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SOME OBSERVATIONS ON CERTAIN BACTERIOLOGICAL AND SEROLOGICAL EXAMINATIONS OF STORED BLOOD.

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NUMEROUS practical problems arise during the maintenance of a "blood bank", and in this paper the results of the investigation of two such problems are reported—the contamination of stored blood and the agglutinability of red cells during storage. The first investigation deals with the incidence of contamination in stored blood. This has already been studied by several workers, including Hunwicke,(1) Elliott, MacFarlane and Vaughan(2) and Boland and co-workers.(3) Differences in general technique and type of apparatus may, however, necessitate the use of variations in the measures taken to prevent contamination, and it should be the responsibility of every person in charge of a "blood bank" not only to devise measures for use with the apparatus provided but also to ascertain whether and to what extent contamination occurs in his particular organization. The results reported in this paper are those obtained in a series of tests on bottles of blood chosen at random from those collected at the "blood bank" established by the Red Cross Blood Transfusion Service at the Walter and Eliza Hall Institute, Royal Melbourne Hospital.

The second investigation was carried out to determine whether the cross-typing results obtained with blood from the small sample tube attached to each bottle were reliable, and whether this sample was representative of the blood stored and administered.

[1] This work was carried out with the aid of a grant from the National Health and Medical Research Council.

Apparatus Used for the Collection of Blood.

The apparatus used in the collection of blood is the standard "Soluvac" blood transfusion set as used by the defence forces and the Red Cross Blood Transfusion Service in Australia. The bottle, which has a capacity of 1,200 cubic centimetres, is fitted with a two-hole rubber stopper, which is sealed with a "Latex" rubber disk, the latter being kept in place with a metal plate and ring, and the whole finally protected with a metal cap. The assembly of the rubber bung and caps both for the collection of blood and for storage is illustrated diagrammatically by Officer.(4) The "taking set" used for the collection of blood consists of two needles joined by 11 to 13 inches of gum rubber tubing and a bung perforator. The bottles are assembled for autoclaving without the outer metal caps, and the metal ring is screwed on till it just engages the thread on the neck of the bottle. The top of the bottle is then covered with two thicknesses of greaseproof paper, which are tied round the neck of the bottle. All apparatus is autoclaved at a pressure of 15 pounds per square inch for twenty minutes. The bottles are allowed to remain in the autoclave for at least ninety minutes after the pressure has dropped to zero. The autoclave is then opened, and as the bottles are being taken out the metal ring is screwed tight (the paper not being removed). The bottles are generally just warm when removed from the autoclave. All other equipment, "taking" and "giving" sets and outer caps, are similarly wrapped and autoclaved. Prior to the collection of blood the "taking" set is assembled and inserted in the bottle and the anticoagulant solution (50 cubic centimetres of a 4% solution of sodium citrate containing glucose, 1%) is added to each bottle. All this work is carried out with aseptic precautions.

After the requisite amount of blood has been collected from the donor, the "bottle" needle is withdrawn from the "Soluvac" bottle and the other needle is kept in the donor's vein until a sample of approximately five cubic centimetres of blood has been collected into a tube containing 0·5 cubic centimetre of 4% sodium citrate solution with glucose (1%). This sample is used for the routine

preliminary bacteriological examination, and portion of the remainder is put into a small sterile corked tube and placed on the outside of the corresponding "Soluvac" bottle. This sample is used for cross-typing.

Contamination of Stored Blood.

Methods.

In order to detect possible contamination before storage, a sample of approximately one cubic centimetre from the blood collected in the tube as described above, was placed in both cooked meat medium and nutrient broth and incubated for seven days. Samples of blood collected from 3,450 donors were treated in this way since the "bank" started in January, 1939. Latterly the procedure has been to incubate the inoculum for two days and to use cooked meat medium only. This procedure is admittedly open to criticism on bacteriological grounds; but it enables all attempts at culture to be examined before distribution of the greater part of the blood stored. If the samples of blood examined in this way were found to be contaminated, the corresponding bottles of blood were withdrawn from the bank, incubated for two days and opened, and samples were placed in cooked meat medium and nutrient broth. These attempts at culture were incubated for two days, smears were then made, examined and subcultured to agar or other suitable media.

As the routine cultural examination is not a true test of the sterility or otherwise of the blood actually stored and administered, and as the number of bottles suspected of contamination is small, some of the bottles of blood normally discarded on account of age were examined. These bottles, which had been stored in the refrigerator for the maximum routine period of twenty-one days without being used, were removed from the refrigerator and allowed to stand at room temperature for periods varying from one to 71 days. They were subsequently incubated at 37° C. for two days. The bottles were then opened and attempts at culture were made as described above for the examination of bottles suspected of contamination. Two bottles, after removal from the refrigerator, were placed immediately in the incubator without a preliminary interval at room temperature. Blood collected from 37 donors was placed immediately after collection in the incubator for two days, while blood collected from 11 donors was allowed to stand at room temperature for one to ten days and subsequently incubated; attempts to grow cultures were then made.

A further series was provided by 22 bottles in which the sealing of the bung by the rubber diaphragm was defective. This defect is due generally to one of two factors: either the metal ring and cap are not sufficiently tightly screwed up to keep the rubber disk and metal plate firm or the glass air tube is too loose around the projecting rubber nipple. In these cases it is found that when the bottles are subjected to any slight variation in temperature —for example, on their removal from the refrigerator—the blood runs up the air tube. If the fitting is very bad, the blood may actually be syphoned out of the bottle. An illustration of this fault is found in the article by Officer.[4] It has been the practice of the "blood bank" to discard such bottles; but as a matter of interest, the contents of 22 such bottles were incubated in order to confirm or refute the danger of these defects in predisposing to contamination.

Results.

It was found that in a series of 125 bottles without obvious defects, but otherwise chosen at random from 2,546 bottles of blood collected under normal conditions, one bottle was contaminated (Table I). This series includes blood cultured immediately after collection, blood cultured after standing at room temperature, and blood cultured after standing at room temperature after twenty-one days' storage. The organism present was a strain of *Staphylococcus aureus*, which gave a negative response to the coagulase test. The attempt at culture made on the sample of blood (corresponding to the bottle) at the time of collection was unsuccessful, so this blood would have been distributed if this investigation had not been proceeding. This failure may be due to the technique used (incubation of the culture material for two days only) or to the fact that the contamination occurred in the bottle. Investigation of samples tested at the time of collection of the blood showed that organisms were present in six samples; but these or any organisms were not found on incubation and attempted culture of the bottle itself.

The second series consists of 22 defective bottles in which blood had travelled up the length of the air tube during storage (Table II). Ten were found to be contaminated, two with *Bacillus subtilis*, seven with strains of *Staphylococcus aureus* (six of which gave a negative response to the coagulase test and one a positive response) and one with a strain of *Staphylococcus albus*. In only two instances in this series did growth occur in the routine attempt at culture (in which an organism corresponding

TABLE I.

Results of Cultural Examination of Bottles of Stored Blood.

Description of Bottles.		Number of Days in Incubator.	Number of Bottles Contaminated.	Number of Routine Cultures Yielding Growth of Organisms.	Remarks.
Number of bottles of fresh blood examined	37	2	Nil.	1	*Staphylococcus aureus* grown in routine culture.[1]
Number of bottles stored at room temperature, then examined ..	11	2	Nil.	1	Gram-negative saprophytic bacilli grown in routine culture.
Stored 1 to 7 days	8			1	
Stored 7 to 10 days	3			Nil.	
Number of bottles stored in refrigerator for 21 days, then examined ..	2	2	Nil.	1[2]	*Staphylococcus aureus* grown in routine culture.[1]
Number of bottles stored in refrigerator for 21 days, then stored at room temperature and examined ..	75	2	1	3[2]	*Bacillus subtilis* grown in two routine cultures. Mixed culture of staphylococci obtained at routine test.
Stood at room temperature—					
1 to 7 days	31		1	2	*Staphylococcus aureus* grown from bottle kept at room temperature one day after refrigeration. Corresponding routine cultural examination yielded no growth.[1]
7 to 14 days	17		Nil.	Nil.	
14 to 21 days	9		Nil.	1	
21 to 28 days	10		Nil.	Nil.	
28 to 35 days	2		Nil.	Nil.	
50 to 71 days	6		Nil.	Nil.	
Total number of bottles examined ..	125				
Total number of bottles contaminated	1				

[1] All these strains of *Staphylococcus aureus* gave a negative response to the coagulase test.

[2] Normally these bottles would be incubated without storage.

TABLE II.

Results of Cultural Examination of Defective Bottles of Stored Blood.

Description of Bottles.		Number of Days in Incubator.	Number of Bottles Contaminated.	Number of Routine Cultures Yielding Growth of Organisms.	Remarks.
Number of bottles of fresh blood examined	3	2	Nil.	Nil.	
Number of bottles of blood stored at room temperature for one to seven days, then examined	2	2	1	1	*Staphylococcus aureus*[1] grown from bottle kept at room temperature for five days. Growth of same organism in routine culture.
Total number of bottles stored in refrigerator for twenty-one days, then stood at room temperature and examined	17	2	9	1	
Stored at room temperature—					
1 to 7 days	7		5	Nil.	*Staphylococcus aureus*[1] grown from five bottles stored at room temperature one, two, four, six and seven days; corresponding routine cultural examination yielded no growth.
7 to 14 days	4		2	1	*Staphylococcus aureus*[2] grown from bottle stored at room temperature for ten days. Corresponding routine cultural examination yielded growth of same organism. *Bacillus subtilis* grown from bottle kept at room temperature for 13 days; corresponding routine cultural examination gave no growth.
14 to 21 days	4		1	Nil.	*Staphylococcus albus* obtained from bottle kept at room temperature for 21 days; corresponding routine cultural examination gave no growth.
49 to 56 days	2		1	Nil.	*Bacillus subtilis* grown from bottle kept at room temperature for 53 days; corresponding routine cultural examination gave no growth.
Total number of bottles examined..	22				
Total number of bottles contaminated	10				

[1] Strains of *Staphylococcus aureus* obtained from bottle and routine culture gave a positive response to the coagulase test.
[2] These strains of *Staphylococcus aureus* gave a negative response to the coagulase test.

to that obtained from the bottle was found). These findings indicate that faulty sealing of the rubber bung is associated with a high rate of contamination. The practice of discarding such defective bottles seems to be a wise and necessary procedure. It should be remembered that with the establishment of "subsidiary banks" in this organization as described in another paper the blood is subjected to variations in atmospheric temperature during transport, and it has been observed that the fault in the bottles sometimes becomes apparent only after they have been subjected to such conditions.

Discussion.

The difficulty of establishing a satisfactory routine for the testing of transfusion fluids for contaminating organisms has been stressed by Logan,[5] who considers that two conflicting ideals are always present, in that it is obviously desirable that bottles should not be opened before use, but also equally desirable that all bottles should be tested for sterility before use. Logan describes a technique for opening and testing bottles before use which, it is held, has never been the cause of contamination of a bottle nor has failed to detect contamination when present.

Although it is realized that the routine technique described in this paper is sometimes unsatisfactory (Table I) and not a true test of the sterility of the contents of the bottle, it is maintained that when rubber diaphragms are used to seal bottles, and such bottles are subject to variations in temperature—for example, storage in a refrigerator—a slight negative pressure always tends to develop. When such bottles are opened there is an inrush of air, and if one is then to wait for the results of a cultural examination, the chance that any organisms thus introduced will grow is increased. When the blood is administered immediately after the bottle has been opened, this is of no consequence. Also it was found on several occasions that although organisms were grown in the cultures of the samples, no organism could be demonstrated in the bottle.

Although it is recommended by Elliott, MacFarlane and Vaughan[3] that the cultures be kept for one week, this procedure has not been followed in this work.

The results obtained in this series by cultural examination of non-defective bottles, with the technique described, do not agree with the statement by Hunwicke[1] that the examination of many specimens of stored transfusion blood shows that complete sterility is a rare condition, and that usually a few organisms are present that do not reveal themselves until the blood has been in the refrigerator for some days or weeks.

Apart from care in the avoidance of contamination during the assembly of the apparatus prior to the collection of the blood, the importance of effective sterilization cannot be overlooked. This problem in connexion with the sterilization of transfusion apparatus, notably bottles fitted with rubber bungs, has received considerable attention from Spooner and Turnbull[6] and from Williams.[7] They maintain that it is necessary to know whether the temperature inside the bottle is high enough, and whether this temperature is maintained for a given length of time. Williams found that dry smears from a slope culture of *Bacillus subtilis* on the inside of a dry bottle survived sterilization for twenty-five minutes at 115° C., and recommended the addition of four cubic centimetres of distilled water to each bottle prior to sterilization. The procedure followed at the "bank" is to dry all glassware in an oven and then assemble and sterilize it. This obviates the leaving of any glassware wet overnight, if there is any difficulty in coping with all glassware that is washed in one day. However, a film of moisture, often forming large drops, is always found in the bottles after sterilization. Therefore, periodically, dry smears from a culture of *Bacilus subtilis* are placed in several bottles, which are then sterilized in the various autoclaves used. Also small capsules containing benzoic acid, which melts at 122° C., are placed inside assembled bottles and sterilized. It should be emphasized that all the bottles submitted to cultural examination (of which the results are given in Table I) were selected at random from over two thousand bottles collected over a period of eighteen months. Similarly, the tests described above for effective sterilization were performed on bottles assembled by any members of the staff. It is realized that the personal element can play a large part in the effectiveness of any technique; but the figures given were obtained during the normal

operation of the "bank" by a large and varied staff, so that this factor need not be considered in this case. The contamination in bottles that normally would have been administered to patients is low and compares favourably with that obtained by Elliott, MacFarlane and Vaughan[2] and by Boland and co-workers[3] in smaller series and when they were establishing their technique.

The high incidence of contamination found in the series of bottles with leaking air tubes showed not only that it was imperative that the assembly of bottles *et cetera* should be checked continuously, but also that when this fault occurs the blood should be discarded.

Sensitivity of Red Cells.

The sensitivity of the red cells of 23 samples of blood stored for various periods from seventeen to thirty-nine days was determined. A comparison was made between the sensitivity of the cells stored in the "Soluvac" bottles and those stored in the small cross-typing tubes.

Methods.

The bottles and small tubes were shaken carefully, a sample was removed from each and made up with 0·9% saline solution to a 1% cell suspension. The measurement of the cell suspension concentration was approximate. The samples used belonged to group A, except for three samples which belonged to group B. The sensitivity was estimated by titrating the cell suspension against serial dilutions of group O serum issued by the Commonwealth Serum Laboratories as testing serum and recording the last dilution in which agglutination was observed at the end of two hours.

Blood-grouping tests were performed by the method described by Bryce and Jakobowicz[5] on blood stored for seventeen to thirty-five days. In 19 cases samples were taken from the bottle and the corresponding cross-typing tube and made up with 0·9% saline solution to a 2% cell suspension. The cell suspension was put up with groups A, B and O testing serum issued by the Commonwealth Serum Laboratories, and the agglutination present after five, ten, fifteen and twenty minutes was recorded. Controls for each series were provided by titrating and grouping samples of blood freshly collected and the same blood kept for twelve hours.

Results.

The sensitivity of the red cells in the cross-typing tube attached to each bottle was found to correspond to that of the cells inside the bottle after storage. The blood is collected into the same anticoagulant solution in both cases, though the proportion of this solution present in the small tubes is generally much higher. Although it is stored under the same conditions, the small volume of blood in the tubes is subject to greater temperature variations than the blood in the bottle, and it is generally found that the blood in such tubes tends to be hæmolysed first. The sensitivity of the stored red cells was found to be less than that of freshly collected cells. When the blood from both bottle and tube was grouped after storage, no difference was observed in the time taken for agglutination to appear provided the sample was not too hæmolysed. However, agglutination appeared more slowly than with freshly collected cells. Agglutination was present in 15 cases in ten minutes, in 17 cases in fifteen minutes and in all cases in twenty minutes. From these figures there appears to be no doubt that cross-typing results with stored blood can be relied upon, and that the samples in the small tube are representative of the blood given.

These results do not agree with the report of Crosbie and Scarborough[9] that there was no apparent change in the agglutinogen content at the end of eight weeks.

Summary.

1. The results obtained from cultural examination of 125 bottles of stored blood selected at random from 2,546 bottles collected are given. Only one bottle was contaminated.

2. When 22 defective bottles were culturally examined, 10 were found to be contaminated.

3. The sensitivity of the red cells in the cross-typing tubes attached to each bottle was found to be the same as the sensitivity of the red cells inside the bottle.

Acknowledgement.

I wish to thank Dr. R. Jakobowicz for her generous assistance and advice.

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ASPIRATION BIOPSY.[1]

By T. E. WILSON, M.D., M.S., B.Sc., M.R.A.C.P., F.R.A.C.S.,
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PERHAPS it is trite to say that successful treatment depends on accuracy in diagnosis; yet the truth of this hackneyed statement does not detract from its importance or from the wisdom of employing ancillary methods of investigation in cases of difficulty or obscurity. During the past two decades sporadic reports of the use of aspiration biopsy have appeared; but, with few notable exceptions, it has been singularly neglected even in appropriate and perplexing cases.

Aspiration of a lesion for the purposes of diagnosis is of value whether organisms, parasites or tissue cells are obtained. In 1909 Horder[1] suggested puncture of the lung as a means of determining the causal organism in pulmonary diseases when sputum was absent. Since then this method has been successfully used by Stewart[2] and by Sappington and Favorite.[3] The detection of parasites in the fluid aspirated from lymph glands has become a well-established method of diagnosis in trypanosomiasis (Yorke[4]), and sternal puncture may be of value in the diagnosis of leishmaniasis (Scott,[5] and Guerschenowitsch and Titoff[6][7]). It is, however, intended to confine this paper to a short discussion of aspiration biopsy of cellular material, the commonly accepted meaning of the term.

Historical Review.

To Guthrie[8] belongs the credit for introducing puncture of lymph glands as a diagnostic method. This subject was followed up by Forkner;[9][10] but aspiration biopsy of other organs was not proposed until 1930, when Martin and Ellis[11] described their method. Three

[1] This work was carried out during the tenure of an Alcock and Alwyn Stewart Scholarship at the University of Melbourne, and during the tenure of a Fellowship in Surgery at the Prince Henry Hospital, Sydney, 1940 and 1941.

years later Stewart[12] reported his impressions derived from the study of material aspirated from 2,500 tumours at the Memorial Hospital, New York, and Martin and Stewart[13] and Martin and Ellis[14] discussed the method from the clinical viewpoint. The last-mentioned authors considered, *inter alia*, that the method was of particular value in differentiating between recurrences of malignant tissue and masses of scar tissue, inflammatory lymphadenopathies, slowly absorbing hæmatomata or traumatic fat necrosis. This method has been adapted by Forster[15] to the diagnosis of cerebral tumours, aspiration being performed through a trephine hole.

Divers instruments, many of them most ingenious, have been invented for extracting tissue fragments through a needle;[9][16][17][18][19][20][21] but the difficulty of handling and preparing sections from the tiny pieces and the limited field available for examination have militated against the success of this method. Less numerous are the variations of technique for the preparation of smears from the aspirated material; most of them are based on the original method of Martin and Ellis.[11]

Sternal biopsy has been recommended for the diagnosis of metastatic tumours by Kreyberg and Poppe[22] Kato and Wachter[23] and Scott,[5] of myelomatosis by Scott[5] and Stewart and Weber,[24] and of Hodgkin's disease by Varadi[25] and Scott.[5] This procedure has been discussed in a previous communication (Wilson[26]). Forkner[10] suggested aspiration of lymph glands for the diagnosis of obscure cases of leuchæmia; but the necessity for this procedure has been obviated by the success of sternal biopsy in these cases.

Radioscopic guidance has been used by Blady[27] to locate relatively inaccessible lesions, such as those of the pelvis, the mediastinum, the vertebræ, or the head or neck of the femur, and is indicated if the lesion is small, or is situated deeply or near important structures.

A procedure akin to aspiration biopsy has been described by Dudgeon and Patrick[28] for the rapid diagnosis of tumours. Their method consists of the preparation of smears from fluid scraped off the cut surface of a tumour, fixed in Schaudinn's fluid, stained with hæmalum and eosin, and mounted in Canada balsam. The advantages of this method, its rapidity and the few materials required, have also been discussed by Dudgeon and Barrett[29] and by Wrigley;[30] but the relative merits and the accuracy of this method compared with the examination of frozen sections remain unsettled. Like aspiration biopsy, Dudgeon's method requires special attention over a series of cases before reliable reports can be given; nevertheless, it is a method which would seem worthy of trial, especially in conditions in which frozen sections are not available.

Method.

If more than one tumour or enlarged lymph gland is available, selection of the site for aspiration depends on the lack of mobility of the lesion, on its size and depth from the surface, and on the juxtaposition of important structures. Generally, it is better to select a cervical than an axillary or inguinal lymph gland. If the patient is very apprehensive, a sedative may be necessary to allay his fears, but this is unusual.

An 18 gauge lumbar puncture needle with a "Luer-Lok" fitting has been found most convenient. A wheal of 1% "Novocain" solution is raised in the skin near, but not over, the lesion if it is attached to the skin, and a small amount of the anæsthetic agent is injected into the subcutaneous tissues. The needle with the obturator in place is inserted through the anæsthetized area and is directed into the lymph gland or tumour, whose position has been carefully defined beforehand, and which, if mobile, is fixed with the thumb and index finger of the left hand. When the needle has been inserted to the correct depth—that is, when the point has penetrated the tissue to be aspirated—the obturator is withdrawn and the syringe is attached. The needle is then advanced and withdrawn in several directions while suction is maintained. Care must be taken that the point of the needle does not pass through the tissue being aspirated. After suction has been maintained for at least a minute the needle is quickly withdrawn. It is imperative that suction be maintained during the withdrawal of the needle, in order that tumour cells are not injected or deposited in the tissues. If blood is obtained, this is discarded and the aspiration is repeated. (In this series no vascular tumour was aspirated; but in such a case Coley, Sharp and Ellis[31] advised that the blood clot be cut into sections by the paraffin method and examined for tumour cells.) If the aspiration has been successful, one or two minims of opaque fluid will be procured. This fluid is deposited on clean glass slides and spread like blood. Fixation is accomplished by gentle warming, and then the films are stained by the Leishman and May-Grünwald-Giemsa methods. Other methods of fixation, as with Schaudinn's fluid or osmic acid vapour, are equally efficacious, but have been used for only a few specimens in this series.

When prepared by this method, malignant cells (Figures I, II and III) are large, irregular and easily damaged. The cytoplasm has a ground-glass appearance, the nucleus is irregular in size, shape, position and arrangement of the chromatin, and is hyperchromatic. There are usually one or more well-defined nucleoli. No importance can be attached to the number of mitotic figures for distinguishing between malignant or innocent tumours. This fact has been reported previously by Cathie.[32] The malignant cells occur singly or in loose sheets, but they do not present the beautiful tessellated appearance of sheets of cells from innocent tumours. The variability and irregularity of malignant cells are their chief characteristic feature; but occasionally similar changes may be found in other cells—for example, in cells from the hyperplastic type of chronic interstitial mastitis or from normal epithelium involved in an acute inflammatory process.

Polymorphonuclear leucocytes, lymphocytes, plasma cells (Figure III), myeloblasts (Figure IV), lymphoblasts (Figure V), monoblasts (Figure VI), the "atypical lymphocytes" of glandular fever (Figure VII), Sternberg-Reed cells (Figure VIII), giant cells of the benign giant cell tumour (Figure IX), megakaryocytes (Figure X) and other cells are all easily recognized in smears. Occasionally osteoclasts are found in smears from bone (*vide* Wilson,[33] Figure IV). Other typical cells, such as those of Gaucher's and Niemann-Pick's diseases, have not been seen in this series; these cells are portrayed and described by Vogel and Bassen[34] and by Morrison and Samwick.[35]

In the interpretation of smears it is necessary to remember the variety of tissues through which the needle has passed. However, the number of normal cells included in the aspirated material should be minimal if an obturator is used when the needle is inserted and the needle is rapidly withdrawn when sufficient material has been obtained.

The necessity of correlating all the information available from the smears has been emphasized by Martin and Ellis,[14] who gave as an example a smear from a mass in the neck exhibiting sloughing squamous epithelium and large sheets of lymphoid tissue in the absence of a known primary tumour. The diagnosis was that of a branchial cyst; a metastatic nodule sufficiently large to yield sloughing squamous cells would have completely replaced the lymphoid elements of the node.

Discussion.

That negative evidence afforded by aspiration biopsy is of no value has been stressed repeatedly,[11][36][37] and this is especially true after a neoplasm has been irradiated[38] or if there is a predominance of fibrous tissue. This fact, and the notorious difficulty of recognizing malignant cells in pleural and peritoneal exudates, have been indirectly responsible for the caution with which aspiration biopsy has been received.

According to Guthrie[8] the essential requirements in the selection of a lymph gland for puncture are as follows: "The gland must be of sufficient size to permit aspiration; tiny shot-like glands are unsuitable for this purpose; the location of the gland should be such as to permit firm fixation and to render injury of important structures improbable." These criteria still hold and are equally

applicable to tumours. If they were fulfilled in all cases, much of the criticism levelled at the use of aspiration biopsy would be refuted. The occasional difficulty or impossibility of establishing a diagnosis from sections, particularly of lymph glands, should make us tolerant of any failure to elucidate the underlying pathology from smears of aspirated material. The recognition of malignant cells as such without determining the type of tumour is often all that may be attained from smears; but, happily, this is usually sufficient. Frequently when a lymph gland is aspirated, we are cognizant of the presence and often of the type of the primary tumour, and aspiration biopsy is employed only to estimate the extent of the spread of metastases. In other cases differentiation between inflammatory and malignant processes, which generally, but not always, is an easy matter, may be all that is required. Aspiration of a cervical lymph gland is of great value in the diagnosis of cases in which there is an undetected primary tumour of the pyriform fossa, thyreoid gland *et cetera*.

The inability of otherwise following the pathological processes or the effect of therapy on many lesions at once indicates reasons for the use of aspiration biopsy. Other reasons include a refusal on the part of the patient to submit to a minor operation, the desirability of confirming the diagnosis of malignancy in cases in which treatment by irradiation is to be given and in which a cure may later be claimed, the biopsy of otherwise inaccessible tumours such as those in the periphery of the lung[39][40][41][42] or the prostate,[10][25][43] the differentiation between malignant and benign lesions—for example, carcinoma of the breast and chronic interstitial mastitis or traumatic fat necrosis, the desire to avoid a scar on the head and neck, and biopsy of a lesion such as a lymphosarcoma or osteogenic sarcoma which may fungate after incision.

Carcinoma of the breast probably constitutes the disease in which the use of biopsy has been most discussed and, incidentally, most criticized. In cases of doubt, surgical biopsy has been practised as a prelude to radical operation; but even this has not received universal acceptance. The virtues and failings of this procedure appear more or less to counterbalance each other, and its use depends on the individual preferences of the surgeon. On the other hand, the advantages of aspirating a mass deep in the breast to distinguish between a cyst and a solid tumour have long been recognized by most surgeons, although many of them have only examined the material obtained macroscopically.

The indications for the use of aspiration biopsy of the breast may be summarized as follows: (i) to differentiate between a carcinoma and a fibroadenoma, chronic interstitial mastitis, traumatic fat necrosis, or thick-walled, deep-seated abscess, especially in a fat breast or in young women during pregnancy or lactation; (ii) to confirm the diagnosis of malignant disease in cases in which treatment by irradiation is to be given; (iii) to eliminate suspicious nodules in the opposite breast before operation. To these may be added the determination of the presence or the extent of the spread of metastases in the regional lymph glands.

Large series of cases are necessary to determine whether the spread of tumours is accelerated by aspiration; but so far these have not been forthcoming. Until then the theoretical objection that the malignant process may spread through the tiny hole made in its capsule by a fine needle must be provisionally admitted, although it is considered unlikely. The other objection, that tumour cells may be deposited along the needle track, is met by the maintenance of suction during the withdrawal of the needle. Even though all evidence is against the spread of a malignant process by aspiration (Greenough[44]) or by exploratory incision (Wood[45]), either procedure must be regarded as meddlesome in cases in which the condition is known to be malignant and in which a radical cure is to be attempted.

Except in the very early and the very late stages, Hodgkin's disease appears to be the disease *par excellence* for diagnosis by aspiration biopsy. The composite picture of Sternberg-Reed cells, endothelial cells, eosinophile cells, lymphocytes, monocytes, fibroblasts and neutrophile leucocytes makes the diagnosis unmistakable and surgical biopsy unnecessary. Rarely, caseous tissue is also obtained. As with other malignant tumours, diagnosis is more difficult after irradiation. It is always better to aspirate the main gland mass than a small outlying gland. The value of aspiration biopsy in the diagnosis of Hodgkin's disease has also been reported by Guthrie,[8] Forkner,[9] Hirschfield,[46] Schilling[47] and Montes.[48]

Since I hold the opinion that, apart from exceptional circumstances, the existence of adenomata of the thyreoid gland, toxic or otherwise, acute thyreotoxicosis or carcinoma of the thyreoid gland constitutes an indication for operation, aspiration biopsy of the thyreoid gland was not performed. When discussing smears obtained from the thyreoid gland, Stewart[12] stated that they were difficult to interpret—a fact which is not surprising when the variability of the pathology of these conditions is borne in mind. Nevertheless, the presence of a localized, retrosternal goitre without signs or symptoms referable to the thyreoid gland might constitute an indication for the use of aspiration biopsy. Such a case has been described by Roholm.[49]

As Stewart[12] observed, a diagnosis of malignant tumour of a salivary gland is unwarranted if it is based solely on the fact that the smear of the tumour contained only epithelium. The differentiation of malignancy from benignancy in these cases depends, as usual, on the characteristics of the cells. Obviously, if mucoid material is also found in the smear, the diagnosis of a "mixed tumour" is more likely.

Sections of lymph glands from patients suffering from infectious mononucleosis present no specific changes (the few reports on this subject are contradictory[50][51]); but smears from these glands contain a few of the "atypical lymphocytes" and are therefore diagnostic. On the other hand, the changes in the bone marrow are more definite. In the four cases of infectious mononucleosis of this series, monocytes, lymphocytes and "atypical lymphocytes" together comprised 48·3%, 52·1%, 57·4% and 62·7% of the marrow cells respectively, whereas very few monocytes or "atypical lymphocytes" were present in the smears of the lymph glands. In none of these cases had anæmia developed, either myelophthisic or leucoerythroblastic—an engaging fact in a disease in which so much of the marrow is replaced. It would be interesting to ascertain whether the anæmia which sometimes develops when the course of a case of infectious mononucleosis is prolonged, has its origin in a greater preponderance of these aberrant cells in the marrow.

Hæmorrhage (especially from the liver), infection and perforation of a hollow viscus may complicate aspiration biopsy, and in certain situations other complications may occur. In the lung, embolism, hæmoptysis or pneumothorax may ensue; but the risks of these complications should be reduced to a minimum by attention to technique. The risk of air embolism is said to be less if the patient is placed in a slight Trendelenburg position.[27][40]

Before concluding, it is well to remark that it is not intended to convey the impression that aspiration biopsy is infallible or that it is without disadvantages. The architecture of a tissue or invasion by the edge of a tumour cannot be recognized, material is removed from only a localized area, it is difficult to obtain a specimen from a fibrotic lesion, and special practice is necessary to interpret the smears. If aspiration biopsy is to gain a permanent place among diagnostic methods, the contraindications to its use must be carefully observed. Unnecessary aspiration of a tumour prior to operation has already been condemned. Care should be exercised to avoid aspirating very vascular tumours or aneurysms, thyreoglossal cysts (owing to the subsequent development of fistulæ), and hydatid cysts (since interference with these cysts may give rise to anaphylactic reactions, spread of the parasites or hæmorrhage). Aspiration of seminomata must be considered unwise because of their proclivity to metastasize and also because of the specificity of the Aschheim-Zondek test in this disease.

Apart from the foregoing discussion, it must not be forgotten that, if the diagnosis is still in doubt after aspiration biopsy, this procedure has in no way affected the possibility of excision of the lesion for the preparation and examination of sections.

Summary.

1. The procedure of aspiration biopsy has been described and discussed, and a complete bibliography is appended.

2. Aspiration biopsy is of value in distinguishing between inflammatory lesions, cysts and innocent and malignant tumours; but it is rarely possible to determine the nature of a malignant tumour by this means. This method is particularly useful for patients who refuse to submit to surgical biopsy, when repeated biopsies are required for academic purposes, for the biopsy of otherwise inaccessible tumours, to determine the presence and the extent of metastases in the regional lymph glands prior to operation, to confirm irrefutably the diagnosis of malignancy in cases in which treatment by irradiation is to be given and in which cures may later be claimed, and for the biopsy of lesions which are particularly prone to fungate after incision.

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EXPERIMENTAL TRANSFUSION WITH MALARIA INFECTED BLOOD.

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IT has long been known that artificial inoculation of malarial parasites produces a type of malaria which is rapidly cured by means of quinine. Not only is quinine a specific cure in such cases, but if given in even small doses at the time of inoculation it acts as an effective method of preventing the onset of malaria.

Yorke and Macfie[1] and James[2] confirmed these facts during extensive malaria therapy in cases of general paralysis of the insane. In their work the majority of injections were carried out subcutaneously, two cubic centimetres of malaria infected blood being used. They estimated that about 100,000,000 parasites were injected. Yorke and Macfie found that thirty grains of quinine per day for three days commencing at the time of inoculation were sufficient to prevent the onset of malaria. James gave ten grains before and ten grains after the injection, with complete success. This success is, of course, in direct contrast to the results obtained when the patient is infected by means of mosquito bites.

The use of potentially malaria infected individuals as donors for blood transfusion has, in the past, been regarded as dangerous, because the patient might develop malaria, and because the presence of parasites might cause effects which would reduce the value of transfusion. But in an emergency it would be foolish to deny the benefit of transfusion to an exsanguinated patient, if the malarial parasites so transmitted could be dealt with effectively by small doses of quinine, and if the immediate effects of such transfusion could be shown to be of a mild nature.

Experimental transfusions have been carried out upon volunteers to determine whether the infection can be controlled, and whether the immediate harmful effects are such that the benefit of transfusion would be nullified. Volunteers were selected from among subjects who had never lived in malaria infected areas. They were given transfusions of malaria infected blood and the effects of the transfusion were studied.

This experimental work has shown that malarial blood containing a limited number of parasites may be transfused without causing more than mild symptoms in the recipient, and no late effects. Malaria was controlled by the administration to the recipient of a standard course of anti-malarial treatment consisting of quinine, "Atebrin" and "Plasmoquine" and beginning immediately after the transfusion was completed. In every case the transfused blood contained a sufficient concentration of parasites to enable a positive diagnosis of malaria to be made after less than fifty fields in a thick blood film had been searched. In practice this would mean that the donor would almost certainly be showing symptoms and signs of a malarial attack.

Details of the Experiments.

The Preparation of Malarial Blood for Transfusion.

A parasite count was made on the blood of a patient who was suffering from malaria and who was of the same blood group as the volunteer recipient. A white cell count was made and the ratio of parasites to white cells was estimated from a blood film; the number of parasites per cubic millimetre could then be calculated.

Blood sufficient in amount to contain approximately 300,000,000 parasites was withdrawn from the malarial patient into a syringe containing sufficient sodium citrate solution to prevent clotting. As an example, if the patient's blood stream contained 25,000 parasites per cubic millimetre, twelve cubic centimetres of blood withdrawn would contain 300,000,000 parasites.

This malarial blood was mixed with 560 cubic centimetres (one pint) of citrated blood from a compatible non-malarial donor. The mixture thus obtained was used in the transfusion given to the uninfected volunteer recipient. Thick films of the mixture were examined for malarial parasites, and in all cases parasites were found to be present after less than fifty fields had been searched with an oil immersion lens.

The Blood Transfusion.

In order to simulate to a small degree the effects of hæmorrhage, the recipients were bled to an amount of up to 750 cubic centimetres or until they showed signs of collapse. The malaria infected blood was then given by the drip method. None of the recipients showed any ill-effects during transfusion. Details of the transfusions are shown in Table I.

After-Treatment of the Recipient.

Blood films were collected and examined for the presence of parasites (i) immediately after transfusion, (ii) thereafter at intervals of four hours for forty-eight hours, (iii) then every day until treatment was completed.

All volunteers were given anti-malarial treatment beginning immediately after the transfusion. Details of treatment varied in each case, but despite this variation in no case did malaria develop. The first volunteer was given ten grains of quinine intravenously and then thirty grains orally per day for three days. The second volunteer was given 0·1 gramme of "Atebrin" per day for twenty days. Although no parasites were found in any blood films, he was then given a routine course of malarial treatment. All other volunteers were given twenty grains of quinine orally immediately after the transfusion and a routine course of malaria therapy commencing the following day.

The routine course of malaria therapy consisted of the following: ten grains of quinine three times a day for three days, followed by "Atebrin" for five days (commencing with 0·6 gramme on the first day and decreasing by 0·1 gramme per day), followed in turn by quinine (15 grains) and "Plasmoquine" (0·03 gramme) per day for three days, finally followed by "Atebrin" (0·1 gramme on each of six days per week for six weeks).

Transfusion of malarial blood by means of the above technique produced no immediate ill-effects, except that symptoms of a mild nature were experienced by the

TABLE I.

Case Number.	Volunteer Recipient.	Cubic Centimetres of Blood Withdrawn.	Reaction.	Infected Blood Given.					
				Parasites per Cubic Millimetre in Blood of Malarial Donor.	Type of Parasite.	Cubic Centimetres of Malarial Blood Used.	Total Parasites in Infected Blood.	Cubic Centimetres of Blood from Uninfected Donor.	Parasites in Mixed Blood.
I	Ss.	750	Pallor and sweating.	25,000	*Plasmodium falciparum.*	15	375,000,000	560	11 in 50 fields.
II	Ss.	700	Nil.	11,200	*Plasmodium falciparum.*	18	201,000,000	560	Present.
III	Dy.	600	Nil.	20,500	*Plasmodium falciparum.*	18	369,000,000	560	5 in 50 fields.
IV	Co.	250	Pallor and sweating.	18,500	*Plasmodium falciparum.*	21	333,000,000	540	2 per field.
V	Cs.	550	Nil.	4,800	*Plasmodium vivax.*	67	319,000,000	500	Present.
VI	Je.	550	Nil.	4,800	*Plasmodium vivax.*	67	319,000,000	500	Present.

TABLE II.

Case Number.	Volunteers.	Immediate Reaction.	Blood Films.			Treatment.	Late Reactions.				
			After Transfusion.	Examined Four Hourly for Forty-eight Hours.	Daily till Treatment Completed.		Time Confined to Bed.	Pyrexia.	Maximum Pulse Rate per Minute.	Headache.	Vomiting.
I	Ss.	Nil.	No parasites.	No parasites.	No parasites. (15 days.)	Quinine, 10 grains intravenously, 30 grains orally, for three days.	2 days.	Up to 101° F., down to normal on fifth day.	90	Mild, several days.	Nil.
II	Ss.	Nil.	No parasites.	No parasites.	No parasites. (24 days.)	"Atebrin", 0·1 gramme daily for twenty days, then routine malaria therapy.	1 day.	100° F. second day, normal fourth day.	104	Slight.	Nil.
III	Dy.	Mild urticaria.	No parasites.	No parasites.	No parasites. (16 days.)	Quinine, 20 grains, then routine malaria therapy.	None.	Up to 101° F., normal fifth day.	86	Very slight.	Nil.
IV	Co.	Nil.	No parasites.	No parasites.	No parasites. (15 days.)	Quinine, 20 grains, then routine malaria therapy.	None.	Up to 101° F., normal fourth day.	108	Slight.	Nil.
V	Cs.	Slight headache.	No parasites.	No parasites.	No parasites. (8 days.)	Quinine, 20 grains, then routine malaria therapy.	3 days.	102° F. first day, normal fifth day.	102	Severe first day, slight two days.	Once, first day.
VI	Je.	Nil.	Benign tertian malaria parasites.	No parasites.	No parasites. (6 days.)	Quinine, 20 grains, then routine malaria therapy.	1 day.	101° F. first day, normal third day.	96	1 day.	Several times first day.

volunteers. During the first twelve hours no patient experienced shivering, chills, pyrexia or aches and pains.

The more remote effects never began during the first twelve hours and rarely before twenty-four hours had elapsed. These remote effects consisted of slight to moderate pyrexia (100° F. to 101° F.) which lasted for one to three days (see Figure I). During this time slight

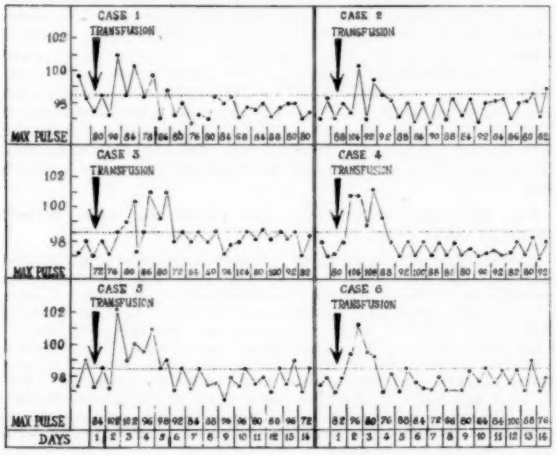

FIGURE I.

malaise and headache were present, but there were no rigors. Some subjects were confined to bed for a short period, mainly because they chose to lie down and were disinclined to do duties in the ward. These reactions were certainly due to the introduced malarial parasites *per se*, as there were no reactions in a series of 100 consecutive transfusions carried out by the same transfusion team with the same technique and non-malarial donors. Moreover, the classical "pyrogen" reactions which are sometimes encountered in transfusion work always occur either during the transfusion or immediately after its completion. No parasites were ever found (except immediately after injection), and no splenomegaly, herpes or subsequent relapses occurred up till one month later. It is probable that the recipients were cured of their malaria, as malaria produced by intravenous injection is easily cured.

Administration of a Transfusion of Potentially Malarial Blood.

Should it be essential to give a transfusion to a patient, using a donor who has a possible malarial infection, the following procedure is recommended.

Examination of the Donor.

(*a*) A general examination of the donor is made to exclude symptoms of active malaria, such as headache, aches and pains and pyrexia. (*b*) The oral temperature is taken, and this should be normal. (*c*) Thick blood films are made, and at least fifty fields are carefully searched for malarial parasites. It is essential that the thick films should be inspected by a trained technician. In the event of the technician's not being an expert in thick film diagnosis, it is far better to use a thin film and make a much more extensive search.

Transfusion Technique.

If all these findings are satisfactory, transfusion can be carried out with any accepted technique, and it is safe to give at least one pint of blood.

The Immediate Institution of Routine Anti-Malarial Treatment.

Routine anti-malarial treatment should be begun immediately the transfusion is completed, and the following drugs and dosages are recommended: quinine (ten grains three times a day for three days), followed by "Atebrin" for five days (commencing with 0·6 gramme on the first day and decreasing by 0·1 gramme per day), followed in turn by quinine (fifteen grains) and "Plasmoquine" (0·03 gramme) per day for three days, finally followed by "Atebrin" (0·1 gramme) on each of six days per week for six weeks. Should the patient be vomiting or should the military situation demand that the patient be evacuated immediately, the intravenous administration of quinine is recommended. Ten grains made up to twenty cubic centimetres with normal saline solution should be injected, at least fifteen minutes being

taken to complete the injection. Rapid injection causes circulatory collapse.

Summary.

Experimental transfusions of malarial blood, containing large numbers of parasites, have been carried out on five volunteer recipients. One volunteer had two such transfusions. The transfusions were immediately followed by routine anti-malarial treatment.

None of the volunteers developed malaria, and no immediate effects were noticed. The more remote effects were not serious enough to cause alarm in any case.

Conclusions.

1. The development of malaria in a non-immune recipient following blood transfusion from an infected donor can be prevented by the immediate institution of anti-malarial therapy.

2. In case of emergency a potentially malarial donor could be used for transfusion, with the knowledge that the benefit derived from the transfusion would far outweigh any ill-effects resulting therefrom; such blood would contain less numerous parasites than the blood used in these experiments, and might contain none.

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EXPERIMENTAL OBSERVATIONS UPON THE LIMITATIONS OF OIL AS A VEHICLE FOR ANÆSTHETIC AGENTS.

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WHEN oil-soluble anæsthetic agents were introduced it was hoped that a method had been discovered at last which would give prolonged relief from pain. Each of these agents consists of a strong solution in oil of an analgesic which is not readily soluble in water. Butesin and benzocaine, under various names, are the drugs commonly used; the former, according to Martindale (1941), is almost insoluble in water, while benzocaine is soluble only to the extent of 1 in 2,500. Both are readily soluble in oil, and the manufacturers reasoned that, since injected olive oil is not absorbed for at least a fortnight, the anæsthetic agent would be liberated slowly, and would produce analgesia for that period.

The first oil-soluble anæsthetic agent to become popular was "A.B.A.", or *Injectio Benzocainæ*, which has the following formula (Martindale):

Benzocaine	3 parts
Benzyl alcohol	5 parts
Ether	10 parts
Olive oil	to 100 parts

It was recommended for neuralgia in which well-defined tender spots could be located, and for fissures and other painful conditions in the anal region. Good results were reported from the beginning. Later some surgeons reported that the use of "A.B.A." was attended by severe pain at the moment of injection, and sometimes for a few days afterwards (Morgan, 1935). Modified products were then introduced, from which the ether was omitted, and a water-soluble anæsthetic was added in order to give immediate analgesia. Two of these are well known. The first is "B.A.B.A.N.", which has the following formula:

Butesin	1 part
Benzocaine	6 parts
Ethocaine	1 part
Benzyl alcohol and olive oil	to 100 parts

The second is "Proctocaine", of which the formula is as follows:

Procaine	1·5 parts
Butesin	6·0 parts
Oil *et cetera*	to 100 parts

Good results have been reported from the use of these formulæ, and the brochures which accompany the products confidently predict analgesia lasting fourteen days.

Personal Experiences.

"A.B.A."

From the first I was unable to convince myself of the value of "A.B.A." in fibrositis. Because of the pain which accompanied the injection, it was necessary to infiltrate the area beforehand with procaine. The tissues into which it had been injected were tender on the day following; this should not be so if the analgesia lasted fourteen days. In one case the injection of "A.B.A." into the thenar eminence was followed by painful swelling of the hand, which lasted a week. Another patient complained of pain during an experimental infiltration of the subcutaneous tissues over the tibia; but within two minutes both skin and periosteum were insensitive to painful stimuli. Next day the sensibility of the skin was normal and the deeper tissues gave a "bruised" feeling on pressure.

"Proctocaine."

In some cases of fibrositis of the sole, the disability can be removed completely (for the duration of the anæsthesia only) by anæsthetizing a localized spot situated deeply in front of the calcaneus. In one such case exactly symmetrical lesions were present in both feet. Three cubic centimetres of a 1% solution of procaine were injected into one lesion, and the same amount of "Proctocaine" into the other. Immediately afterwards the patient felt no pain or tenderness. On the following day the symptoms had returned with added intensity in both feet.

The following experiment was performed upon myself on three occasions:

Three cubic centimetres of "Proctocaine" were introduced into the subcutaneous tissues over the tibia to occupy a circular area three inches in diameter. The area of skin, which was slightly bulged by the oil, became totally anæsthetic within thirty seconds, as also did the underlying periosteum. The anæsthesia lasted only three hours, however, and from then onwards the skin sensation was normal, while the periosteum was tender to pressure. The oil was distinctly visible for more than a week, and though the subcutaneous tissues pitted on pressure, no diminution of cutaneous sensation could be detected. This area of skin was itchy for a few days.

"B.A.B.A.N."

The same procedure as that employed with "Proctocaine" resulted in anæsthesia which lasted three hours. Aching pain followed, which remained for twenty-four hours. On the following day the skin was red and the periosteum was tender to pressure. For three days the skin was itchy. The oil disappeared within a week.

Discussion.

The foregoing observations seem to indicate beyond doubt that the effect of oil-soluble analgesics lasts for no more than a few hours. It is known, however, that the injection of watery solutions of procaine sometimes gives

ILLUSTRATIONS TO THE ARTICLE BY DR. T. E. WILSON.

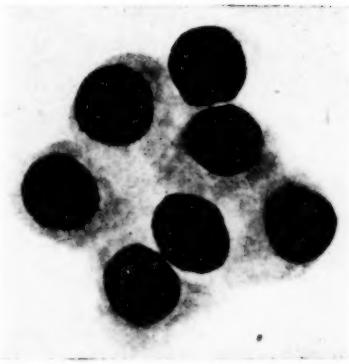

FIGURE I.

A group of malignant cells from an axillary gland. The primary tumour of the breast had been present for at least six months.

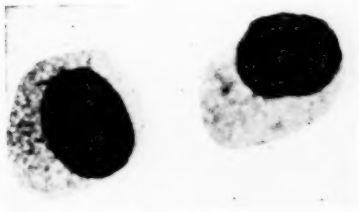

FIGURE II.

Two malignant cells aspirated from a nodule on the chest wall. This patient, aged thirty-two years, presented many similar nodules from one to eight centimetres in diameter which were situated in the subcutaneous tissues, and which had been present for at least five years. The cells aspirated from the tumour were unquestionably malignant, and notwithstanding the length of history, the diagnosis of malignant melanoma was later made from a section of the mass that had been aspirated.

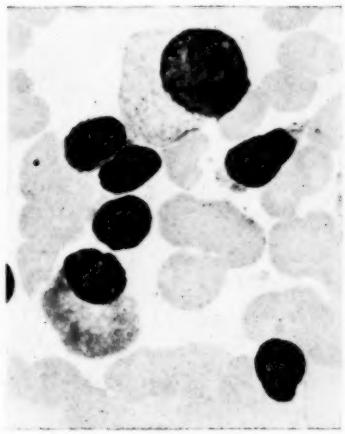

FIGURE III.

A group of lymphocytes, a plasma cell and a malignant cell present in a smear from a submaxillary lymph gland of a patient with a carcinoma of the lip.

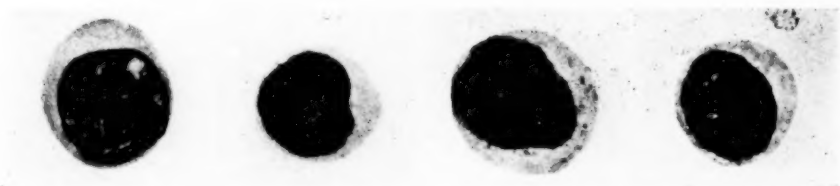

FIGURE IV.

A myeloblast from a lymph gland of a patient with chronic myeloid leuchæmia.

FIGURE V.

A lymphoblast from a lymph gland of a patient with chronic lymphatic leuchæmia.

FIGURE VI.

A monoblast from a lymph gland of a patient with acute monocytic leuchæmia.

FIGURE VII.

An "atypical lymphocyte" from a lymph gland of a patient with infectious mononucleosis.

FIGURE VIII.

A Sternberg-Reed cell of Hodgkin's disease from an acute case, in which death occurred within two months of the onset of symptoms.

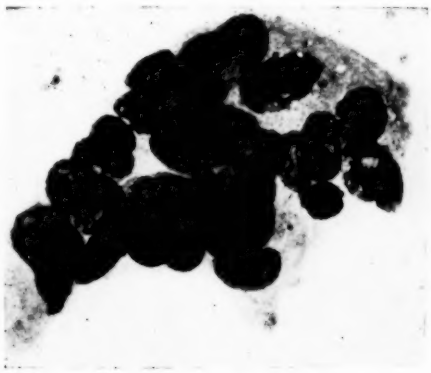

FIGURE IX.

A giant cell from a benign giant cell tumour of the upper end of the tibia.

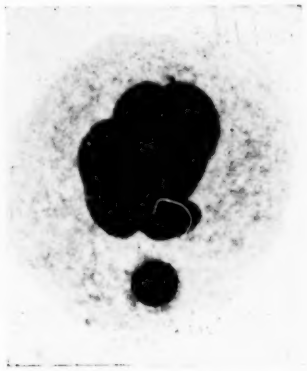

FIGURE X.

A megakaryocyte from a lymph gland of a patient with chronic myeloid leuchæmia. The cytoplasm of this cell contains the phagocytosed nucleus of a lymphocyte.

ILLUSTRATIONS TO THE ARTICLE BY DR. JAMES ISBISTER.

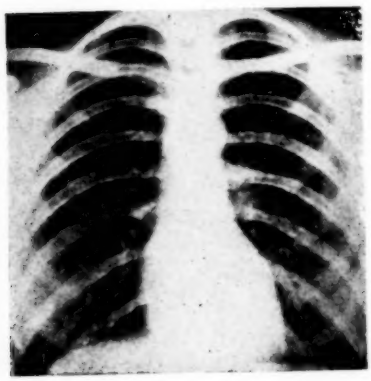

FIGURE I.

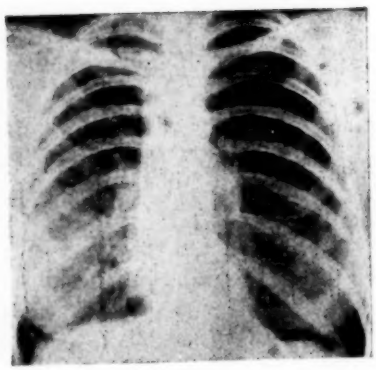

FIGURE II.

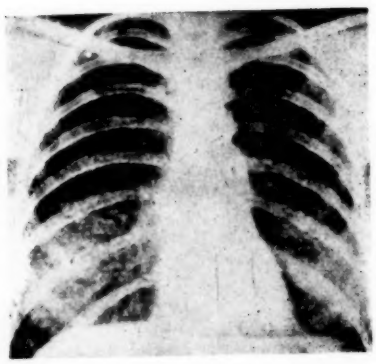

FIGURE III.

lasting relief from pain. The good results which sometimes follow the use of oily solutions may thus be attributable to the factor which operates in the case of aqueous solutions. In all probability, a critical follow-up of a number of cases would indicate that neither *pruritus ani*, nor pain after operations on the anus, is influenced by these agents.

Is Oil of any Value as a Vehicle?

Deansley and Parkes (1933) first introduced the use of oil as a vehicle for the injection of hormones, the advantage claimed being that the product was absorbed evenly over a period of fourteen days. Earlier, oil had been used as a solvent for camphor injected intramuscularly. Later oil became popular as a vehicle for the introduction of such toxic and irritant agents as gold salts, for which slow absorption was necessary, for the injection of adrenaline in obstinate cases of asthma, and for many other drugs.

More recently, however, dissatisfaction with oil has been expressed by Bray (1943), who reports that it is an unreliable vehicle for adrenaline. Absorption may be as rapid, he says, as that from watery solutions, and deaths have been reported from overdosage. Freyberg (1942), who has used gold salts extensively for arthritis, states that the insoluble salts are not absorbed at all, whether suspended in water or in oil, and that the absorption of the soluble salts is only slightly delayed by the use of oil as a vehicle.

The Effects of Oil on the Tissues.

Emery, Matthews and Schwabe (1942), Emery and Matthews (1943), and Brown, Wilder and Schwartz (1944) have extensively investigated both the absorption of theelin and stilbœstrol from oily solutions, and the local effects upon the tissues of various oils. All the commonly used oils were injected intramuscularly into hundreds of rats, and examinations of the tissues were conducted at varying intervals up to a year. Blood assays indicated that the drugs were absorbed in an unpredictable fashion, and the authors regard the method as completely unreliable. Local irritation of muscular tissues was produced in every case, and in some cases the inflammation preceded the formation of sterile abscesses. In the majority of the rats the oil became encysted, the cysts persisting sometimes for as long as a year. In subcutaneous tissues, these authors report, irritation was less and absorption was more rapid. In man, however, occasional cases are reported of pathological effects upon the subcutaneous tissues (Conrad, Conrad and Weiss, 1943).

The commonest use of oil solutions in therapeutics is the treatment of hæmorrhoids with phenol in almond oil, the object of which is to produce a pathological reaction which results in shrinkage of the tissues. It is possible that the oil is equally effective as the phenol in producing this reaction; cases have been reported in which granulomatous tumours and other undesirable effects have been produced (Jackman, 1940; Ackland, 1944; Levy and Horn, 1944).

It is well known that the intrathecal use of lipiodol is sometimes followed by irritative effects and chronic inflammation of the tissues (Craig, 1929; Boldrey and Aird, 1944). Perhaps the blame for this should be laid upon the oil itself, which acts as a foreign body, rather than upon the iodine, which is a chemical component of the molecule.

Summary.

1. The analgesia which results from the use of oil-soluble anæsthetic agents lasts no longer than a few hours.

2. The use of oil as a vehicle in parenteral therapy is attended by two disadvantages: (*a*) the rate of absorption of the drugs is inconstant; (*b*) oil itself acts as a foreign body in the tissues.

Acknowledgement.

The Director-General of Medical Services, Australian Military Forces, has kindly permitted the publication of this article.

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Reports of Cases.

A CASE OF BESNIER-BOECK-SCHAUMANN SYNDROME, OR BENIGN LYMPHO-GRANULOMATOSIS, WITH PNEUMOTHORACES.

By JAMES ISBISTER,
Squadron Leader, Royal Australian Air Force.

THE Besnier-Boeck-Schaumann syndrome is known by a variety of names, the most familiar of which are those that form the title of this report and, more shortly, sarcoidosis. The true ætiology of this disease is unknown, and some authorities even state that it is an atypical form of tuberculosis. It affects chiefly the reticulo-endothelial and lymphatic systems, being characterized mainly by diffuse infiltration of the lungs, enlargement of the lymphatic glands and spleen, and involvement of the skin and eye. It is usually confused with tuberculosis, Hodgkin's disease or other forms of lymphadenopathy. For a comprehensive review of the disease the reader is referred to an article by Hannesson,[6] or to one that appeared in this journal by Lambie.[3] The following case is reported because it presents a clinical feature or complication hitherto undescribed, that of pneumothorax. A search of the literature in the English language has failed to reveal a previously reported case of pneumothorax occurring in this condition.

Clinical Record.

The patient, P.K., a female, first came under medical observation in December, 1940, at the age of nineteen years. There was no history of relevant previous illnesses. At that time she complained of loss of weight (about two stone), loss of energy, and insomnia, progressing over a period of four to six months. She had had amenorrhœa for two months, and for a few days before being examined had apparently had a "cold". On examination she was found to have a temperature of 101° F., but apart from her "thin" appearance there were no other abnormal physical findings. Radiographic examination of her chest revealed "very extensive

discrete infiltration through both lungs of productive type, especially right—almost certainly pulmonary tuberculosis" (Figure I).

The erythrocytes numbered 4,780,000 per cubic millimetre and the hæmoglobin value was 13·0 grammes *per centum*. The leucocytes numbered 4,900 per cubic millimetre, and were distributed as follows: 64% were neutrophile cells, 25% were lymphocytes, 9% were monocytes and 2% were eosinophile cells. An Arneth count revealed a shift to the left, 15% of the neutrophile cells being band forms. An examination of the sputum on two occasions revealed no tubercle bacilli.

For the next year she was kept under observation and her general condition gradually improved. She gained one stone in weight, and serial radiographic examinations of her chest revealed a progressive resolution of the appearances previously described in the lungs. During this phase a diagnosis of Besnier-Boeck-Schaumann syndrome was made, based on the course of the disease, on the radiographic appearances of the lungs, and on the failure to find tubercle bacilli in the sputum. In January, 1943, she enlisted in the Women's Australian Auxiliary Air Force. Her general condition was good, she was capable of playing tennis without distress, and a photofluorograph of her chest on a 35 millimetre film was passed as normal. A subsequent radiograph on a full-sized film revealed traces only of the pulmonary infiltration.

She was quite well until two months prior to her admission to an air force hospital in October, 1943. She began to complain of dyspnœa on exertion and of pain in the left side of her chest. Clinical examination then revealed signs of a left-sided pneumothorax, and this was confirmed radiographically; the film showed a partial pneumothorax on the left side, causing displacement of the heart, and also a diffuse mottling or "marbling" of both lung fields, especially towards the basal regions (Figure II). On comparison with previous X-ray films, the mottling was more pronounced even than in the original film taken almost three years previously. The erythrocytes numbered 4,600,000 per cubic millimetre, and the hæmoglobin value was 11·4 grammes *per centum*; the leucocytes numbered 8,900 per cubic millimetre, 79% being neutrophile cells, 14% lymphocytes, 4% monocytes, 2% eosinophile cells, and 1% basophile cells. The neutrophile cells were mature. The erythrocyte sedimentation rate was seven millimetres in one hour. No tubercle bacilli were found in six specimens of sputum, nor were they found by smear or by cultural examination of the fasting gastric contents. A Mantoux skin sensitivity test, carried out with one in 1,000 strength old tuberculin, gave a negative result. Radiographic examination of the hands and feet revealed a small cystic area on the head of the left first metatarsal bone, and another at the base of the proximal phalanx of the second digit of the same foot. The Wassermann test failed to produce a reaction. The fasting blood serum protein content was 8·5 grammes *per centum*, of which the albumin fraction was 6·2 grammes *per centum* and the globulin fraction 2·3 grammes *per centum*.

After two weeks' rest in bed the left lung had fully expanded clinically and radiologically. After a total of a month in hospital the patient was discharged for convalescence. She was then capable of normal exertion without dyspnœa. Two weeks after leaving hospital, whilst at rest, she suddenly complained of pain in the right side of the chest and of dyspnœa. Following this episode she again noticed dyspnœa on exertion as before. Clinical examination revealed signs of a right-sided pneumothorax. This was confirmed radiologically; a partial right pneumothorax was found with approximately the same degree of lung collapse as had previously occurred on the left side. The heart was correspondingly displaced to the left (Figure III). After two and a half weeks' rest in bed the right lung was fully expanded clinically and radiologically. Since then the patient has remained well, and no other clinical manifestations of the disease have occurred. A radiograph of the chest in May, 1944, revealed a slight decrease in the mottling compared with that found at the previous examination in December, 1943.

Discussion.

The case presented has been diagnosed as one of Besnier-Boeck-Schaumann syndrome. In most recorded cases of this disease the diagnosis has been confirmed by histological study of material, usually an excised lymph gland. Longcope[9] has reported a series of 31 cases, and in 29 of these some or all groups of superficial lymph glands were affected. So it appears to be uncommon not to have some enlarged glands, but in the reported case a careful search was made on several occasions, and no palpable glands were observed. This naturally precluded the possibility of taking material for biopsy. Schaumann[11] found in his series that in all cases in which a tonsillectomy was performed the typical histological picture was found in the tonsil. His "diagnostic triad" consisted of examination of the tonsil, a negative response to the Mantoux test, and cystic areas in the bones of the hands and feet on radiological examination. He therefore suggested tonsillectomy as a diagnostic aid in cases in which no lymph glands were suitable for biopsy. However, tonsillectomy was not performed in this case. The diagnosis was therefore made on the course of the illness, on the radiographic appearances of the lungs, on the radiographic evidence of bony involvement, on a raised serum protein level, and on a negative response to the Mantoux test. These criteria, together with other interesting features of the case, will therefore be discussed in detail.

The course of the disease is typically one of relapse followed by resolution affecting various organs and parts of the body, often one after the other. The present case shows this, at least as far as the lungs are concerned, since there was a gradual resolution over the first three years, followed by a fairly rapid relapse radiographically coincident with the pneumothoraces. This is now apparently being followed again by resolution. As yet no other organs appear to have been affected apart from bones. The length of the course tends to rule out the original diagnosis of miliary tuberculosis, although healing in cases of this disease are stated to occur.

The radiological appearance of the lungs in this case is typical of the disease; the films show a diffuse "marbling" effect more pronounced in the basal than in the apical zones. King[7] has reviewed in 112 proved cases the radiographic appearances and the course of the affection in the lungs. He states that the earliest change is enlargement of the mediastinal lymph glands. Then the characteristic infiltration of the lungs occurs, with either a "marbling" effect or a more localized lesion resembling miliary tuberculosis. As this change takes place, the enlargement of the hilar glands subsides again, and then finally the change in the parenchyma of the lungs resolves, sometimes leaving an appearance suggestive of fibrosis. Of his 112 cases, in 50 the X-ray films were characteristic skiagraphs, and 37 of these patients were followed up; in 23 the condition had cleared completely, or nearly so, in up to three years; in three it had not completely cleared in one, two and a half and three years respectively, but continued to do so; in eight there was no change in three months to four years, and in three spread occurred after seven months, eight months, and four years respectively. The last case was unique, and closely resembles the case reported, in that the condition had apparently cleared but recurred after the four years. This was the only one of its type in the series, and the question of a superimposed tuberculous infection was raised. To refer back to the enlargement of the hilar glands, in Longcope's[9] series of 31 cases this was noted in 26, and in 29 there was evidence of pulmonary involvement. There was no evident enlargement of these glands in the present case.

Radiographic evidence of bony involvement in this case is interesting, as it is the main point confirming the diagnosis, and it has not been noted in other cases reported in Australia. Lambie[3] reported eight cases, Frank[2] seven cases, and Hurley and Hughes[5] two cases; although most of these patients had their hands and feet radiographically examined, no evidence of bony involvement was found in any of them. Although bones may be involved without radiographic evidence, the typical appearance is punched-out cyst-like area of bone absorption towards the ends of the phalanges, described originally by Jungling[6] under the title of *"osteitis tuberculosa multiplex cystica"*, and it is often associated with an overlying skin lesion of *lupus pernio*. Jungling was under the mistaken impression that it was tuberculosis. Lambie[3] states that this manifestation may rarely occur in this country on account of the temperate climate, and that it is commoner in colder climates.

The total serum protein content in this disease is usually raised above the normal maximum of 7·5 grammes *per centum*. This is due mainly to a rise in the globulin fraction, the albumin remaining about normal. This rise of serum protein level is common in most diseases involving the reticulo-endothelial tissues of the bone marrow. Longcope[9] found in 18 cases that the globulin fraction was above the average normal of 2·58 grammes *per centum* in all cases; the albumin content was below the average normal of 4·44 grammes *per centum* in 13 cases. In most of his cases the total serum protein content was above normal. Salvesen[10]

found an increase in the total serum protein content of 9·0 to 9·69 grammes *per centum* in three out of four cases, again owing mainly to an increase in the globulin fraction. In the present case there was an increase in the total serum protein content, but it was due mainly to an increase in the albumin fraction. It is considered that the latter finding is of no significance, as the figures for the different fractions vary considerably according to the method of estimation used.

The Mantoux test in this case produced no reaction, and this helped to distinguish the disease from miliary tuberculosis, although sometimes in the latter the reaction ultimately fails to be elicited. However, sarcoidosis appears to render the patient unusually resistant to the test, and the large majority of patients fail to react to it. Frank[3] reported six such failures to react to the Mantoux test in seven cases, and Longcope[9] 22 failures in 26 cases. Brook and Day[1] reported on this test in detail, and found four failures to react to it in seven cases, when one in 1,000 strength old tuberculin was used. These figures give a higher proportion of failures to react to the Mantoux test than one would expect in the general population. As well, every effort was made without success to discover the tubercle bacillus in the sputum and gastric contents.

The blood counts performed in this case on two occasions gave results within normal limits, apart from a "shift to the left" revealed by the count performed in December, 1940. Frank[3] reported three cases associated with a "shift to the left", one associated with eosinophilia and three associated with monocytosis in a series of seven cases. Longcope[9] states that if anything is characteristic in the blood picture, it is eosinophilia. Schaumann[13] mentions as typical a "shift to the left" of the neutrophile cells and a monocytosis.

Finally a word must be said about the pathology and its possible relation to the pneumothorax. Histologically the typical picture is one of a granulomatous lesion. Epithelioid cells are arranged usually concentrically, and there are a few lymphocytes on the periphery and a few giant cells of variable type. There is little if any evidence of a surrounding inflammatory reaction, and necrosis is not a feature of the histological findings. If necrosis is present, it may lead one to suspect superimposed tuberculosis, though Schaumann[12] stated that small caseous centres might be found in foci otherwise presenting a typical sarcoid structure and not indicating a tuberculous infection. In healing, the sarcoid nodule either resolves and disappears completely or may become replaced by fibrous tissue. It is therefore difficult to explain the occurrence of pneumothorax. Possible explanations are obstruction to a terminal bronchiole with alveolar emphysema leading to rupture into the pleural cavity, necrosis of a subpleural focus, or superimposed tuberculosis. The occurrence of bilateral pneumothoraces coincident with an increase in the parenchymal infiltration and no evidence of tuberculosis can reasonably be explained only as due to the sarcoidosis. Practically every part of the body can be affected, and other parts more commonly involved are the skin, the eye, the spleen, the liver and more rarely the heart and brain. Longcope[9] in his series of 31 cases reported involvement of the skin in 16 cases, of the eyes in 16, of the spleen in 15, and of the liver in 13. None of these parts appeared to be affected in the present case.

The prognosis in this disease is usually considered to be good, and cases reported in Australia bear this out. However, some subjects have come to autopsy without other complicating diseases. This occurs when vital organs such as the heart, pituitary, or brain are involved. Cameron and Dawson[2] review the course and prognosis, based on a case report, and emphasize how there might be relapses followed by resolution affecting one organ after another over a period of years. They state that in most fatal cases death has been due to superimposed pulmonary tuberculosis, though other modes of death are pulmonary fibrosis with failure of the right side of the heart, destruction of the hæmatopoietic tissues, and localization in vital areas. Tice and Sweaney[14] have reported the autopsy findings in a case in which failure of the right side of the heart occurred as a result of a condition resembling Ayerza's disease with *endarteritis obliterans* of the pulmonary arteries following sarcoidosis. Therefore, in the case cited, one should be optimistic regarding the prognosis with the reservation that these considerations indicate.

With reference to treatment, apart from the rest in bed while the lungs were deflated, no special methods were used. It is doubtful if any treatment has any effect on the course of the illness. Frank[3] used radiotherapy in three of his cases with benefit, causing diminution in the size of lymph glands. Other authorities state that radiotherapy has no effect on glandular enlargement and may even be harmful in the case of the mediastinal group. Other forms of treatment that have been used are arsenic given by mouth, gold injections, chaulmoogra oil, and large doses of vitamin *C*.

Summary.

1. A case of the Besnier-Boeck-Schaumann syndrome with bilateral pneumothoraces is reported and discussed.

2. The diagnosis was made on (*a*) the course of the disease, (*b*) the radiographic appearances of the lungs, (*c*) the radiographic evidence of bony involvement, (*d*) an increase of total serum protein content, (*e*) failure to react to the Mantoux test and (*f*) failure to isolate tubercle bacilli.

No biopsy material was available to confirm the diagnosis.

3. The pathology, prognosis and treatment are briefly discussed.

Acknowledgements.

I wish to thank the Director-General of Medical Services, Royal Australian Air Force, for permission to publish this report. I also thank Group Captain G. C. Willcocks and Professor C. G. Lambie for their help and advice. My thanks are also due to Dr. Bruce White on behalf of Dr. Cotter Harvey, Dr. A. J. Hood Stobo and Dr. K. E. Shellshear for permission to use the clinical notes and radiographs of the patient prior to her enlistment in the Women's Australian Auxiliary Air Force.

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(5) L. E. Hurley and J. F. Hughes: "Besnier-Boeck-Schaumann Syndrome: A Discussion with a Report of Two Cases", THE MEDICAL JOURNAL OF AUSTRALIA, September 12, 1942, page 238.

(6) O. Jungling: Quoted by C. G. Lambie, *loco citato*.

(7) D. S. King: "Sarcoid Disease as Revealed in the Chest Roentgenogram", *American Journal of Roentgenology and Radium Therapy*, Volume XLV, April, 1941, page 505.

(8) C. G. Lambie: "Besnier-Boeck Disease or Benign Lymphogranulomatosis of Schaumann (The Besnier-Boeck-Schaumann Syndrome)", THE MEDICAL JOURNAL OF AUSTRALIA, June 15, 1940, page 815.

(9) W. T. Longcope: "Sarcoidosis or Besnier-Boeck-Schaumann Disease", *The Journal of the American Medical Association*, Volume CXVII, October 18, 1941, page 1321.

(10) H. A. Salvesen: Quoted by H. Hannesson, *loco citato*.

(11) J. Schaumann: "Benign Lymphogranuloma and its Cutaneous Manifestations", *The British Journal of Dermatology and Syphilis*, Volume XXXVI, December, 1924, page 515.

(12) J. Schaumann: Quoted by H. Hannesson, *loco citato*.

(13) J. Schaumann: Quoted by C. Cameron and E. K. Dawson, *loco citato*.

(14) F. Tice and H. C. Sweaney: "A Fatal Case of Besnier-Boeck-Schaumann Disease with Autopsy Findings", *Annals of Internal Medicine*, Volume XV, September, 1941, page 597.

Reviews.

LECTURES IN DISEASES OF CHILDREN.

DR. ALAN MONCRIEFF is determined not to allow Sir Robert Hutchison's well-known work to lose its high position in pædiatric literature, for even the war has not prevented him from revising the lectures in the ninth edition, recently published.[1] A veritable fund of information is available here

[1] "Lectures on Diseases of Children", by Sir Robert Hutchison, Bart., M.D., LL.D., F.R.C.P., and Alan Moncrieff, M.D., F.R.C.P.; Ninth Edition; 1944. London: Edward Arnold and Company. 8½" × 5½", pp. 485, with many illustrations. Price: 21s. net.

for the experienced practitioner as well as for the beginner. The book has unquestionably stood the test of time and will always rank high in the list of books recommended to the student of pædiatrics. Its value is only likely to be enhanced by Dr. Moncrieff's able editorship, as can readily be seen by the quality of the additions to this edition. These include short succinct accounts of infections in the newborn, the treatment of infantile diarrhœa, the cause and treatment of cœliac disease, and the Rh factor. The quality and clarity of the illustrations remain extraordinarily high.

In our review of the eighth edition we pointed out minor discrepancies in that volume. To these it might be added that a palpable spleen is compatible with normal health in spite of the author's contention. In this country rickets would not receive such prominence, and the anterior fontanelle closes much earlier than "between the eighteenth and twenty-fourth month". In these hectic days few mothers would heed the advice to feed their infants every three hours instead of every four hours until they are three months old. The inclusion of a photograph of a seven-year-old child to illustrate pemphigus of the newborn is not a happy one. Similarity of environment plays a greater part in the family predisposition to rheumatic fever than heredity. Finally, though "growing pains" is an unsatisfactory term, no attempt is made to distinguish muscular and fascial pains occurring in children associated with climatic changes, debility and fatigue from the true joint pains of rheumatic fever. However, these points detract in no way from the general excellence of the book, and it is hoped that Dr. Moncrieff will continue to keep it at the front rank of medical "best sellers".

THE SEVENTH ADDENDUM TO THE BRITISH PHARMACOPŒIA, 1932.

ON February 1, 1945, the General Medical Council released the Seventh Addendum to the British Pharmacopœia, 1932, and it will have official status in Great Britain from that date.[1] It contains twenty-seven new monographs in addition to a general section devoted to tablets and many modifications of existing monographs.

One-third of the new monographs deal with the sulphonamides—sulphapyridine, sulphacetamide, sulphadiazine and sulphathiazole, together with their soluble forms, and sulphaguanidine. A uniform dose of 8 to 30 grains (0·5 to 2·0 grammes) is quoted for all of them, including sulphaguanidine, despite the more heroic doses usually advocated for the guanidine derivative. Directions for their sterilization, both in powder and in solution, are given. The insoluble forms, with the exception of sulphacetamide, are also included as tablets.

The newer barbiturates are represented by the rapidly acting soluble pentobarbitone ("Nembutal")—one and a half to three grains—and its thio-derivative, soluble thiopentone ("Pentothal Sodium"), for which the intravenous dose is quoted as one and a half to five grains.

Strophanthin-G ("Ouabain"), obtained from the seeds of the *Strophanthus gratus* and from the wood of *Acokanthera schimperi*, is added to the official cardiotonic glycosides, the dose being 1/500 to 1/120 grain. In view of its greater toxicity—reputed to be twice that of Strophanthinum B.P., obtained from the seeds of *Strophanthus kombe*—it would almost seem advisable to amend the name of the latter to "strophanthin-K." lest confusion arise.

Hormone products include the "natural" œstrogens, œstradiol monobenzoate (1/600 to 1/12 grain) and œstrone (1/600 to 1/6 grain), and the *corpus luteum* product, progesterone (1/60 to 1/12 grain by injection). Androgens of the testosterone type, though included in the British Pharmaceutical Codex, have not as yet found a place in the British Pharmacopœia.

Anæsthetic drugs comprise the gas cyclopropane (trimethylene) and amethocaine hydrochloride—a local anæsthetic of the procaine series. In the case of amethocaine, no guide is given with regard to dosage or to the concentrations of solutions which combine effectiveness with safety.

[1] "Seventh Addendum to the British Pharmacopœia, 1932", published under the direction of the General Council of Medical Education and Registration of the United Kingdom; 1945. London: Constable and Company Limited. Pp. 113.

The synthetic sympathomimetic amine, amphetamine (benzedrine), and its orally administered derivative amphetamine sulphate, are also subjects of new monographs. For the base, which is a volatile mobile liquid administered by inhalation, no dose is quoted. For the sulphate the dose is 1/12 to 1/6 grain.

The remaining new monographs deal with dextrose monohydrate (medicinal glucose), injection of protamine zinc insulin having a standard strength of 40 units per millilitre, anticoagulant solution of sodium citrate, solution of sodium citrate with dextrose, potassium sulphate, theophylline with ethylene-diamine (one and a half to five grains), and two new ointments. These ointments—*Unguentum Hydrargyri Ammoniati Aquosum* and *Unguentum Zinci Oxidi Aquosum*—are both made with the hydrous ointment base (Sixth Addendum). The corresponding non-hydrous ointments of ammoniated mercury and of zinc are also retained but with a simple ointment base.

In a general monograph, devoted to tablets, are outlined acceptable processes of manufacture, standards for uniformity of weight and a disintegration test. This is followed by monographs dealing with thirty-five different tablets, each carrying a footnote defining the dose of the drug per tablet that will be dispensed or supplied should the dose not be specified on the prescription or order. Some lack of uniformity will be noted in this, in that some are defined in grains and some in fractions of a gramme.

In the following list of tablets, the defined doses are quoted.

Acetylsalicylic acid	5 grains
Ascorbic acid	0·05 gramme
Nicotinic acid	0·05 gramme
Atropine sulphate	1/100 grain
Barbitone	5 grains
Soluble barbitone	5 grains
Calcium lactate	5 grains
Carbromal	5 grains
Codeine phosphate	½ grain
Ephedrine hydrochloride	½ grain
Glyceryl trinitrate	1/130 grain
Hexamine	5 grains
Mercury with chalk	1 grain
Mercurous chloride	1 grain
Mepacrine hydrochloride	0·1 gramme
Nicotinamide	0·05 gramme
Phenacetin	5 grains
Phenobarbitone	½ grain
Soluble phenobarbitone	½ grain
Phenazone	5 grains
Phenolphthalein	2 grains
Potassium bromide	5 grains
Potassium chlorate	5 grains
Quinine bisulphate	5 grains
Quinine hydrochloride	5 grains
Soda mint	——
Sodium salicylate	5 grains
Stilbœstrol	0·0005 gramme
Sulphadiazine	0·5 gramme
Sulphaguanidine	0·5 gramme
Sulphanilamide	0·5 gramme
Sulphapyridine	0·5 gramme
Sulphathiazole	0·5 gramme

The various amendments to existing monographs are for the most part modifications which concern the manufacturer rather than the prescriber. In the cases of menaphthone and stilbœstrol the modes of sterilization are specified. *Belladonnæ Folium* now becomes *Belladonnæ Herba*, and its liquid extract acquires the unwieldy name of *Extractum Belladonnæ Herbæ Liquidum*. Similarly liquid extract of colchicum, hitherto made from the seed, may be made from the corn and becomes *Extractum Colchici Cormi Liquidum*. Happily there are no alterations in the strengths of alkaloids in the corresponding preparations, and it is made clear that the right extract will be dispensed if the prescriber merely orders *Ext. Bellad. Liq.* or *Ext. Colch. Liq.*

Ext. Pituitarii Liq. is required to bear a label stating the number of units (oxytocic) per millilitre, but in an appendix, details for its standardization in terms of antidiuretic and of pressor units are given, and these may also be stated on the label.

A very useful addition is a cumulative index to all the addenda.

The Medical Journal of Australia

SATURDAY, MARCH 17, 1945.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

NEUROFIBROMATOSIS AND OSTEITIS FIBROSA CYSTICA.

To remark that when many names are found attached to a clinical condition its true nature and origin have not been determined beyond reasonable doubt, is to be trite. However, that gaps still exist in our knowledge of many disease conditions is not to be wondered at, seeing that the human body is complex and many of its tissues are highly specialized and seeing that the bacterial and other agents which may affect them are numerous and act in many different ways. Rather might we wonder that a certain agent affecting body tissues produces a pathological pattern that presents little variation in different individuals or in the same individual at different times. When a student of disease discovers that a syndrome or what he regards as a syndrome is not always constant, but that variations are found in certain of the examples, he quite naturally tries to find a name which in his opinion will distinguish the special examples that he has discovered from the larger and commonly recognized groups. Sometimes the new name is justified; sometimes it is not, and it is in this way and perhaps also because some investigators merely try to be different that the Babel of names is increased and terminology becomes more confounded. The use of eponyms does not solve the problem, for an eponym is a starting point and not infrequently calls for some alteration; and, moreover, one author may have his name given to more than one disease. The name of von Recklinghausen is a case in point. On the one hand there is von Recklinghausen's disease commonly known as neurofibromatosis; on the other hand we have von Recklinghausen's disease of bone. These two conditions are full of interest both to the pathologist and to the clinician. Though at first sight there appears to be no reason why any confusion in regard to them should occur, they present certain features which call for close study and discernment if a proper understanding is to be gained.

The condition known as neurofibromatosis, or sometimes as von Recklinghuasen's disease, was described by that author in 1882. Kinnier Wilson gives a straight-forward account of it and points out that skin, bone, endocrine glands and nervous system are the seat of congenital disorders that characterize it. These disorders comprise pigmented flecks and spots on the skin, multiple neurofibromata of cranial and peripheral nerves, cutaneous fibromata of different kinds (including hypertrophy of different parts), spinal curvature, bony overgrowth or softening and periosteal thickening. Diverse endocrine syndromes are a frequent complication, as well as the occurrence of heterogeneous tumour formation in the nervous system. In discussing the pathology of the condition, Wilson names four characteristic features—neurofibromata, pigmentary lesions, skeletal lesions and associated developmental anomalies. In regard to skeletal lesions, Wilson draws attention to the hyperostosis of subcutaneous and periosteal fibromata, and adds that the bones of the chest have been found to have become relatively soft, as a result of which considerable deformity may occur. Sometimes there is a degree of dorso-lumbar or cervico-dorsal kyphosis or kyphoscoliosis, the head being sunk between the shoulders, the sternum being bent or folded and the pelvis asymmetrical. Wilson thinks that it would be misleading to describe the condition as osteomalacia or *osteitis fibrosa*, but recalls the fact that local bone changes resembling subperiosteal cysts can sometimes be discovered by X-ray examination. He quotes other authors to show that the cystic appearance of the bone may continue and that the bone may become more porous and plastic, lengthened and bowed as well as roughened and pitted. Spontaneous fractures may occur. Von Recklinghausen's disease of bone or generalized *osteitis fibrosa et cystica* is described in text-books as one of the diseases of bone resulting from a disorder of calcium metabolism and calcification. It is due to overactivity of the parathyreoids and as a rule is caused by hyperplasia or a tumour of one or both glands. Most of the bones are affected, but not all to the same degree. The bones become soft and consequently bending and extreme deformities of the long bones and spine occur. Beattie and Dickson point out that pseudocysts are formed and that microscopically the contents of the cysts are seen to consist of a mixture of blood corpuscles, fibroblasts and giant cells. "The lesions result from the decalcification and resorption of existing bone, and its replacement by an osteoid and fibrous matrix in which inefficient attempts at calcification take place. . . . The marrow also undergoes fibrous change. . . . The development of giant cell tumours . . . is not uncommon and, by some authors, is regarded as a characteristic feature of the disease." When the tumour of the parathyreoid gland is removed the disease is arrested and resumption of normal calcification takes place.

Before further discussion is undertaken regarding the two conditions bearing von Recklinghausen's name, reference must be made to another condition described by Louis Lichtenstein in 1938 as polyostotic fibrous dysplasia.[1] This condition is, he states, a skeletal developmental anomaly affecting several or many bones and having a predominantly unilateral involvement. He has found what he regards as cases of polyostotic dysplasia described in the literature under an amazing array of names—*osteodystrophia fibrosa unilateralis*, unilateral polyostotic *osteitis fibrosa*, unilateral Recklinghausen's disease, *osteodystrophia fibrosa cystica generalisata* limited to one side of the body, focal *osteitis fibrosa*, *osteitis fibrosa* in multiple foci, *osteitis fibrosa* with formation of hyaline cartilage,

[1] *Archives of Surgery*, Volume XXXVI, 1938, page 874.

osteitis fibrosa disseminata. The characteristic pathological feature of this condition is stated to be "a disturbed function or development of the bone-forming mesenchyme, resulting in the filling of the medullary cavity of affected bones by fibrous tissue, in which spicules of poorly calcified primitive fiber bone are developed by osseous metaplasia". The bones on X-ray examination cast a shadow of diminished density, "suggesting a rarefied or porotic trabeculated lesion, replacing bone and usually interpreted as indicating cystic disease". The condition with which it is often confused is, Lichtenstein remarks, von Recklinghausen's disease of bone. In a subsequent communication Lichtenstein and H. L. Jaffe drew attention to occasional non-skeletal aspects of the condition, including pigmentation of the skin,[1] and also emphasized the need for its differentiation from hyperparathyreoidism accompanied by skeletal involvement.

A study has recently been published by S. J. Thannhauser in which he discusses a common pathogenesis of neurofibromatosis and *osteitis fibrosa cystica localisata et disseminata* (both conditions bearing the name of von Recklinghausen) and in which he distinguishes between the latter condition and hyperparathyreoidism with generalized decalcification and fibrocystic changes of the skeleton. Thannhauser attaches importance to investigations by Masson, reported in 1942, in which he showed that fibromata in neurofibromatosis may not show their derivation from schwannoglia by the presence of nerve tissue within the fibromatous masses. Therefore the lack of nerve tissue in fibromatous masses does not disprove their neurofibromatous origin. The finding of aneuritic fibromata in organs other than the skin, together with neurofibromatous involvement of the skin, is very suggestive of a common histogenesis for the two features. When whorls of spindle cells are present in the fibrous tissue they indicate its neurofibromatous origin. Thannhauser discusses the pigmented areas of skin with sharp borders (these are the *"café au lait"* spots or geographical map-like brown blotches) and shows that they are the result of structural changes of the underlying smallest skin nerves. These pigmented blotches "are as much an indication for the diagnosis of neurofibromatosis as the cutaneous neurofibromatous nodule itself". In regard to the fibrocystic involvement of localized areas of the skeleton, especially of the long bones, but also of other portions, which occurs in neurofibromatosis, Thannhauser points out that osseous fibromata are found not only as so-called subperiosteal cysts, but also as fibromata located in the trabeculated spaces of the long bones. Microscopic examination of the osseous fibroma does not reveal nerve structure within the fibroma, but whorls of spindle cells appear in certain areas to indicate its neurofibromatous origin. At this stage of the discussion attention should be directed to Albright's work on *osteitis fibrosa cystica.* This condition was commonly regarded as a result of hyperparathyreoidism in spite of the fact that many cases of the disease have not been characterized by parathyreoid enlargement, increased calcium levels in the serum, generalized demineralization of the skeleton, or calcium metastases. Albright, recognizing this, drew a distinction between *osteitis fibrosa cystica disseminata* and *osteitis fibrosa cystica generalisata.* He reserved the former title for those cases in which localized and disseminated lesions of the skeleton are present with normally calcified and normally structured bones. He reserved the latter for the cases of generalized demineralization of the skeleton, with fibrocystic lesions. In the former normal calcium and phosphate and only slightly increased phosphatase values are found; in the latter high calcium and low phosphorus levels are found in the serum with high phosphatase values. Thannhauser asserts that the condition described by Lichtenstein and Jaffe as polyostotic fibrous dysplasia is *osteitis fibrosa cystica disseminata.* According to his views that have been quoted on fibrous tissue, pigmented spots and so on, he would appear to be justified in this view. His main conclusion is that neurofibromatosis and *osteitis fibrosa cystica disseminata* have a related pathogenesis. This means that he accepts Albright's classification and makes a clear distinction between the condition which he relates to neurofibromatosis, and *osteitis fibrosa cystica generalisata* or hyperparathyreoidism with generalized decalcification and fibrocystic changes of the skeleton.

In conclusion, let us follow Thannhauser further. He refers to von Recklinghausen's paper of 1892 and points out that of the sixteen cases described by him, three (V, VI and VII) are supposed to represent the clinical and anatomical features of "Recklinghausen's bone disease". He is at some pains to show that Cases V and VI, described as fibrous osteitis, exhibit the features of *osteitis fibrosa cystica disseminata.* On this account he thinks that the name of von Recklinghausen should be associated with that condition and not with hyperparathyreoidism. This is all very well, but in Thannhauser's description of Recklinghausen's Case VII mention is made of a structure above the left thyreoid gland which might have been a parathyreoid tumour (Jung). Although it was not until 1925 that Collip reported his studies of the parathyreoid hormone and until 1926 that Mandl removed an adenomatous parathyreoid gland from a patient suffering from *osteitis fibrosa cystica,* this restriction of von Recklinghausen's name will not find general acceptance. This really brings up the whole question of the use of eponyms. There are those who would do away with them on the grounds of accuracy and science. Others, more humanistic maybe or more devoted to an historical view of medicine, prefer to retain them, even though different names are used for the same malady in different countries and though on occasion two or even three names have to be strung together to indicate a syndrome.

[1] *Archives of Pathology,* Volume XXXIII, 1942, page 777.

Current Comment.

FALLACIES IN SEROLOGICAL TESTS FOR SYPHILIS.

THE complement fixation test which usually bears the name of Wassermann has maintained a strikingly important position in the diagnosis of syphilis for nearly forty years. It survived the shock of being found to be specific in the chemical sense only and not truly in the immunological sense. It rose from being a mere adjunct to clinical diagnosis to the not entirely tenable role of being the ultimate word; and now, reinforced by the various flocculation tests, it is still an invaluable piece of evidence, though there are fallacies in its results. Of these fallacies the so-called "false positive" is the reaction which causes some worry. It is known that certain other diseases may cause serum reactions to this test, such as yaws, leprosy,

malaria and other tropical conditions; infectious mononucleosis, tuberculosis and atypical pneumonia and certain other infective and metabolic disturbances are also reported as causing similar changes in the physical state of the blood serum.

But of much greater importance is the "false positive" given by the serum of a person subjected to routine test when there is no obvious disturbing factor. Fortunately this very rarely occurs with the cerebro-spinal fluid. But the problem, though not often seriously arising in practice, is not statistically negligible, as Dr. Bernard Davis points out in a recent survey of this question, and in support he quotes Kahn's disturbing figures.[1] Thus if 5% of a population were syphilitic, a laboratory test which was 99·5% specific and 80% sensitive would give 0·5% false positive results and 4·0% true positive results. If then treatment were undertaken on the serological evidence alone, one-ninth of the patients treated would needlessly be subjected to treatment. Davis reminds us that the substance reacting in the serum is not truly an antibody, and is better called a "reagin", though it is not certain that the well-known reinforcing effect of cholesterol when added to the antigen is entirely passive from the immunological viewpoint. The false positive which interests us most is that due to the existence of some changed state in the patient's serum, which, though unrelated to true antibodies, may yet produce flocculation or complement fixation reactions. We need not here enter into discussion of the obscure mechanisms involved. Of course, for over a generation serologists have laboured so to modify the complement fixation test as to make it both highly specific and highly sensitive. International conferences have been held in the attempt to settle the question and mountainous statistics have been compiled to help to a decision. The introduction of the various flocculation tests, with their high degree of specificity, has done much to assist in this difficult subject. The use of immunologically specific antigens, that is, those actually prepared from the *Treponema pallidum*, has not made a great deal of headway for routine work. Davis's article has some interesting sections on verification tests. He points out that a reliable verification test should not give an appreciable number of "false negative" results, that is, it must have a sensitivity at least equal to that of standard diagnostic tests. An analysis of "verification" tests, in particular those brought forward by Kahn, has been made by Mohr and others in a review of the recent additions to knowledge on syphilis.[2] It would appear that while a study of certain phenomena observed by Kahn promises to cast light on the mechanism of these tests, it is premature to assume that a true "verification" test exists. The problem is therefore not yet entirely solved. Still, we must adopt certain safeguards, and Davis suggests the following procedure. First, an exhaustive and careful history and physical examination are essential, next, any possible basis for a false response must be sought and eliminated, then the marital partner, children and siblings should be tested, tests of the patient's serum must be repeated immediately to exclude error, and such tests should be quantitative. The last point is important, for the "*plus* 2, *plus* 3 or even *plus* 4" result is apt to be illusory, since it only records the strength of a reaction in one standard dilution of the serum. To these precautions are added a period of probation or delay after which the test is repeated, for the "false positive" may be a transient phenomenon. Lastly, the cerebro-spinal fluid should be tested and supplementary tests such as flocculation tests applied.

Davis sagely remarks that the occurrence of a reaction to the complement fixation or flocculation tests for syphilis is not an emergency.

Recently in this journal Neil W. Francis and James S. Wannan have recorded their experiences with the intensive treatment of syphilis, and their article contains some valuable remarks on the false positive problem.[3] They point out that flocculation tests are usually more sensitive than the Wassermann test, and in the false positive group the comparative results with the two tests are apt to be contradictory. Further, the titre of the serum yielding such reactions usually decreases rapidly. Perhaps, as they state, there is a tendency to over-emphasis on the sensitivity of the serological tests. But it is most important to remember that the occasional surprise caused by the disclosure that a patient's serum unexpectedly reacts to these specific tests should also evoke caution and scepticism. Repeated and multiple tests are necessary, time must be taken to establish a diagnosis, and in making this important decision, which might in rare cases disrupt the life of some luckless person, the art of the clinician must not be forgotten.

[1] *Medicine*, December, 1944.
[2] *Archives of Internal Medicine*, November, 1944.
[3] THE MEDICAL JOURNAL OF AUSTRALIA, February 24, 1945.

THE ROYAL SOCIETY OF TASMANIA.

THE Royal Society of Tasmania was founded on October 14, 1843. In honour of its centenary it has published a centenary number of its *Papers and Proceedings*. The volume, a substantial production of some 250 pages, has been edited by Dr. Joseph Pearson, the honorary secretary and the librarian of the society, and by D. Colbron Pearse. The objects of the society as set out in the original rules were "to develop the physical character of the island, and illustrate its natural history and productions". In 1907 the rules were altered and it was declared that "the objects of the society are the prosecution of the study of science in its various branches, and more especially the development of a knowledge of the physical characters and natural history of Tasmania and the neighbouring States". Since 1914 the object of the society has been "the advancement of knowledge". The scientific activities of the society have covered zoology, botany, geology, paleontology, natural science, anthropology and history, and papers have been presented at its meetings by many notable workers. Since 1845 reports have been published, and since 1850 reports and papers have been published together. The centenary number contains a long treatise by Professor G. E. Nicholls on the Phreatoicoidea, Professor Eric Ashby discusses a century of ideas on evolution, Professor V. V. Hickman writes on some new Australian Apneumonomorphæ and their respiratory systems, Winifred M. Curtis writes on variation in *Pultenæa juniperina* Labill and J. Somerville on the history of the society. Sir Ernest Clark, Governor of Tasmania, is president of the society and takes an active interest in its proceedings. He succeeds a long line of governors who have held the office since Sir J. E. Eardley Wilmot, Lieutenant-Governor of Van Diemen's Land, founder of the society, became its first president.

The Royal Society of Tasmania has had important links with medicine in that island. We read that in 1896 seventeen members established a medical section, prominent members of which were G. H. Butler, E. L. Crowther, A. H. Clarke and G. Sprott. "Many highly technical papers were read and discussed at the sectional meetings, whilst medical subjects of a more general nature were brought before the society and public interest aroused in the health of the community." Activities continued until 1912, the section receiving an annual grant of £12 for the purchase of medical books. We also read that the "Southern Branch of the B.M.A. affiliated with the Section in 1912". This is intended to refer to the Tasmanian Branch which was formed on July 22, 1911. There was no southern division of the Branch, and the Tasmanian Branch has no record of any actual affiliation. The relations between the two bodies have, however, always been most cordial and the annual meetings of the Branch are still held in the Royal Society's library.

Among the activities of the Royal Society of Tasmania is the control of the Botanical Gardens and the Tasmanian Museum, where its library is also housed. To these activities must be added the publication of the *Papers and Proceedings*, a scientific journal of which the society has every reason to be proud. That this journal has been able to continue its publication during the war and to maintain its high standard must give the council of the society much satisfaction; it also speaks well for the Tasmanian Government which helps to meet the cost. We offer the Royal Society of Tasmania our congratulations on the appearance of the centenary number of its journal.

Abstracts from Medical Literature.

RADIOLOGY.

Tuberculous Pulmonary Cavitation Tending to Heal Spontaneously.

LASAR DUNNER (*British Journal of Radiology*, September, 1944) describes a particular type of tuberculous "cavitation complex" in the lung, different from both the early and late cavity. The appearances to be noted in the X-ray film are those due to (*a*) the cavity itself, and (*b*) the tuberculosis of the lung associated with it. Both of these show distinctive characters. They are to be taken together and regarded as the two constituent parts of an entity, hereinafter to be named the "cavitation complex". The film presents the usual typical ring shadow of a lung cavity, the wall of which is as a rule thin and presumably flexible; there is no translucency. The cavity has been seen to occur in various regions of the lung. The second constituent of the "cavitation complex" shows itself as a "spread" of numerous discrete small foci closely grouped in a remarkably regular and even manner. Some variations of this picture may, however, be seen. Thus, in four cases the individual foci were small nodules of the "miliary" type. In six others of the series the even distribution of the foci was disturbed by a sparse scattering of larger foci which probably arise by confluence or enlargement of the smaller ones. But these larger among the smaller foci do not destroy the striking impression of evenness which is characteristic of this "cavitation complex". The appearance suggests a blood-borne rather than a bronchogenic spread. Such a spread may establish itself in any part of the lung and its extent may vary; two or more regions in the lungs may be simultaneously affected in this way. The cavity is situated either within the spread or at its margin. The retrogression of the spread did not entirely correspond with that of the cavity. True, the disappearance of both spread and cavity was found on the same film; but in some the spread terminated later than the cavity. Radiological findings after disappearance of the cavity vary. There may be complete resolution, replacement by a fibrotic scar or replacement by calcification. When the treatment of these cases is under consideration it is to be remembered that the "cavitation complex" may terminate spontaneously. Active therapeutic measures may, therefore, in such cases be held in reserve.

Adenoma of the Bronchus.

THOMAS LOWRY AND LEO G. RIGLER (*Radiology*, September, 1944) describe the clinical and radiological features of adenoma of the bronchus, and discuss briefly its pathology and potential malignancy. A diagnosis of bronchial adenoma is usually rather easily established by radiological and bronchoscopic examination once the condition is suspected. X-ray examination presents two types of evidence with regard to benign bronchial tumours. The first, which was the only evidence available until recently, relates largely to the secondary effects of the obstruction. Thus atelectasis commonly accompanied by the "drowned lung" phenomenon is a frequent finding; especially characteristic is its tendency to be intermittent and recurrent. The atelectasis may be band-like, producing linear areas of increased density, with some general decrease in the radiability of the lung. More commonly it is lobar in type, with a whole lobe collapsed down into a paravertebral triangle of increased density, while the remainder of the lung on that side exhibits greater radiability than normal owing to the expansion of the uninvolved lobes. Secondly, the presence of pneumonitis, which is likewise remittent and recurrent, is suggestive. In this case, rather than the sharply demarcated dense shadow of an atelectatic lobe, there is an irregularly distributed non-homogeneous density in the area of involvement suggesting somewhat the appearance of atypical pneumonia. Finally, the demonstration in simple skiagrams or by means of bronchography of bronchiectasis localized to one lobe should always suggest the possibility of a bronchial adenoma. The demonstration of a mediastinal mass resembling a tumour, with associated evidences of bronchial obstruction, should likewise lead to further investigation, because of the possibility of an extrabronchial extension of such a tumour. The addition of bronchography with iodized oil makes it possible to demonstrate with reasonable accuracy the presence of the associated bronchiectasis and the location of the obstruction. Finally, the use of body section radiography during the past five years has permitted the direct visualization of the tumour itself as a rounded, sharply defined dense shadow seen in contrast to the air in the bronchus which surrounds it. Unfortunately, it is not always possible to make this demonstration satisfactorily. Evidence is presented in favour of regarding this tumour as a clinical entity separate from bronchiogenic cancer, even though the two cannot always be distinguished pathologically, and in spite of the rare instances in which adenoma gives rise to cancer. The chief reason for this division is a practical one: adenoma of the bronchus has a prognosis quite different from that of cancer, and therefore permits the employment of a more conservative plan of therapy in properly selected cases when radical resection would be attended by a large risk.

The Diagnosis of Hypertrophic Pyloric Stenosis in Infants.

H. W. HEFKE (*Radiology*, September, 1944) states that in hypertrophic pyloric stenosis the pylorus and duodenal cap are, as expected, very small, and can be seen only seldom in routine postero-anterior radiographs. It is practically always possible to see them in right oblique and right lateral views. The pyloric opening time is of considerable importance for X-ray examination. A normal pylorus in an infant will open and discharge barium into the duodenum practically always during feeding. When two ounces of a mixture of barium and feeding formula are given, barium is seen to have passed the pylorus in less than five minutes after the feeding is finished. If the pyloric opening time is delayed longer than five minutes, the presumptive diagnosis of pyloric stenosis becomes very likely. In most cases of pyloric stenosis the opening time is found to be between fifteen and sixty minutes. In very early cases it is occasionally normal; in very advanced cases it may be delayed up to three hours, with no barium seen in the duodenum or small intestines at that time. The emptying of the stomach in infants of two to four weeks old is normally between two and four hours when two ounces of a barium mixture are given. At times a little barium is seen in the stomach after a longer interval. It is of much less importance in the diagnosis of pyloric stenosis than it is given credit for in the literature. Of course, when no barium at all has left the stomach in two or three hours, the diagnosis of pyloric stenosis is most likely, that representing a marked delay in the pyloric opening time. In many cases of proved disease with large tumours the opening time of the pylorus was considerably delayed, up to one hour, and yet the emptying time of the stomach was entirely normal; that is, in three to four hours no barium remained in the stomach. Not always do the first two or three films show the narrowed canal. At least a minimal amount of barium must have left the stomach for demonstration of the pylorus and duodenal cap. If the pylorus does not open during the time of fluoroscopy and while the first set of films are being exposed, another series of films is taken in thirty minutes, and still another one hour afterwards. In practically all cases the pylorus and at least part of the duodenal cap can be seen on at least one, usually more than one, film. If a normal opening time of the pylorus and a normal size, length and width of the pylorus and prepyloric region are demonstrable by fluoroscopy, done five minutes after the feeding is finished, and are shown in the first films, no further films are considered necessary, as the emptying time in such cases is of no interest, except for the rare occurrence of duodenal obstruction, which may be picked out by that time and by clinical impression.

Pulmonary Disease Associated with Mega-Œsophagus.

H. STEPHEN WEENS (*American Journal of Roentgenology and Radium Therapy*, November, 1944) demonstrates the association of mega-œsophagus with pulmonary lesions, such as lung abscess, aspiration pneumonitis, pulmonary fibrosis and bronchiectasis. It is believed that the pulmonary lesions are the result of aspiration of œsophageal contents. The incidence of pulmonary lesions in patients with mega-œsophagus is thought to be higher than is generally appreciated. The author has demonstrated pulmonary disease in five out of fifteen cases of mega-œsophagus.

Rib Fractures in Atypical Pneumonia.

ROLFE M. HARVEY (*American Journal of Roentgenology and Radium Therapy*, November, 1944) noted eighteen cases of fractured ribs in a review of five hundred consecutive cases of atypical pneumonia. In nine of these cases the fractures were multiple; in four cases the fractures occurred in the anterior

axillary or axillary line. The reason for this is postulated as due to the opposing forces of the *serratus anterior* and *externus obliquus abdominis* muscles. The occurrence of rib fractures was not related to the severity of the pneumonia. Associated with atypical pneumonias is a severe, dry, irritating cough, which is probably a factor in the production of the fractures. Excessive chest pain occurring in cases of atypical pneumonia should direct the search of the radiologist toward this complication.

Parasternal Diaphragmatic Hernia.

MAX RITVO AND O. S. PETERSON, JUNIOR (*American Journal of Roentgenology and Radium Therapy*, October, 1944), state that parasternal diaphragmatic hernia is a relatively rare lesion, but is of unusual interest to the radiologist as he is usually the only person capable of demonstrating the condition prior to operation or autopsy. On X-ray study in the lateral projection the mass occupies the anterior and mid-portions of the right lower lung field and presents rounded, smooth superior and posterior margins; the anterior border merges with the shadow of the anterior chest wall. In every case with this type of shadow the possibility of parasternal hernia must be considered in the differential diagnosis and a tentative diagnosis of parasternal hernia should be made until proved otherwise. The mass does not pulsate and cannot be separated from the right border of the heart shadow. Fluid levels present within the colonic loops may closely simulate encapsulated pleural fluid or abscess. Barium enema studies are more satisfactory than the opaque meal examination in the demonstration of the lesion.

PHYSICAL THERAPY.

Malignant Tumours of the Kidney: Review of 117 Cases.

LOUIS C. BIXLER, K. W. STENSTROM AND C. D. CREEVY (*Radiology*, April, 1944) discuss 117 malignant renal neoplasms seen at the University of Minnesota Hospitals from 1935 to 1940 inclusive. The group is made up of 94 adenocarcinomata of the cortex (81 proved histologically), 13 Wilms's tumours (5 proved), 9 carcinomata of the renal pelvis (7 proved) and one proved sarcoma. The clinical picture of renal cancer is presented with a brief discussion with the more common symptoms. In spite of improvements in methods of treatment, the mortality from malignant lesions of the kidney remains high. Apparently the greatest obstacle to the reduction of this high mortality rate is the advanced stage of the lesion when the patient is first seen. Hæmaturia is the symptom most likely to make the patient seek advice in time for an early diagnosis to be made. Every patient, therefore, with unexplained hæmaturia should be given a thorough urological investigation. Nephrectomy is the treatment of choice for malignant tumours of the kidney, with the possible exception of Wilms's tumour. In Wilms's tumour irradiation seems to be of greater value than with any other renal neoplasm, and should constitute an important part of the therapy. X-ray therapy is a valuable adjunct to surgery, (*a*) facilitating the nephrectomy in many cases by reducing the size of the tumour, (*b*) perhaps rendering malignant cells dormant and reducing the danger of metastasis from surgical manipulation, (*c*) inhibiting the growth of malignant cells which may be left behind. In cases not suitable for surgery and without metastases, X-ray therapy may be invaluable in prolonging life and affording alleviation. It is also of value in the treatment of late metastases and recurrence as relief of pain is frequently obtained. In this series of cases surgery alone was used in 17 cases, surgery *plus* irradiation was used in 38 cases, and irradiation alone in 13 cases. In adenocarcinoma of the cortex the five years' survival rate for patients treated by surgery alone was 50%; by surgery *plus* irradiation, 31%; by surgery *plus* immediate post-operative irradiation, 42%; by irradiation alone, 8% (77% of patients had metastases at time of diagnosis). In the Wilms's tumour group there were no five-year survivors. Three patients, however, are still living and well with no evidence of disease, the longest period since treatment was carried out being four years and eight months.

Dosage Rate in Radiotherapy.

F. ELLIS (*British Journal of Radiology*, November, 1944) discusses the biological effect of variation of dosage rate in radiotherapy—that is, the rate at which the radiation is delivered during actual exposure. He reviews in detail the experiments of many workers in this field, in which certain biological test objects, tissue cultures and animal tissues have been subjected to radiation at different dosage rates. It is first important to decide whether there is any difference in biological effect corresponding to differences in dosage rate; and, secondly, if there is a difference, what, if any, are the critical values of dosage rate above and below which the effects are different. Holthusen in 1933 published curves showing that for a dosage rate greater than about 5 *r* per minute the epilation effect on human skin is independent of the dosage rate, but that below that rate the effect decreases with diminished dosage rate. The corresponding critical values for skin tolerance and erythema must from his curves be 500 *r* per minute or more. While laboratory experiments appear to be quite valid in offering evidence on the fundamental problems, those on the human skin could be subjected to considerable criticism, which would appear legitimate. The author points out that the dosage rate problem arose chiefly because Coutard's results of treatment of carcinoma of the larynx and pharynx had been published, and in his method a dosage rate of 4 *r* per minute and fractionation of the treatment over a long period were considered essential. Coutard, however, had not been able to use a higher dosage rate because of the limitations of his apparatus. The author is convinced that cancer of the larynx can be cured with a high dosage rate. To those short of apparatus for the number of patients it is wasteful to use a low dosage rate. The economic factor and increased efficiency of apparatus are important. Also the advantages of the rapid treatment from the point of view of setting up the patient are manifest. It is easy to hold for a few minutes a position which would be impossible for an hour. In the successful treatment of rectal carcinoma by the million volt apparatus at Saint Bartholomew's Hospital, London, a high dosage rate and a penetrating beam producing results not duplicated anywhere else are combined. The advent of contact therapy appeared to make the wave-length and dosage rate problems no longer of practical importance, since it is possible to cure skin cancer, cancer of the lip, eyelids and even larynx with dosage rates of 9,000 *r* per minute to 250 *r* per minute. The author concludes that a high dosage rate is a desirable feature of treatment from both the practical and fundamental points of view, except that in the case of radium work the necessary handling without screenage increases the unavoidable dose to the staff. From consideration of the mechanism of action of radiation on cells, both the direct effect on the chromosomes and the indirect effect on cell metabolism, it would appear that a high intensity or dosage rate is advantageous.

The Effect of Radiation Therapy in Clostridium Infection in Sheep.

E. A. MERRITT, A. J. DEN AND U. V. WILCOX (*Radiology*, October, 1944) have attempted to demonstrate the effects of radiation therapy in gas gangrene by animal experimentation. Sheep were chosen for the experiment because these animals are quite uniformly susceptible to *Clostridium* infection; they approximate man in size and weight, they are available and comparatively easily handled, and when taken out of a flock they have a common sire and an almost identical age. A strain of *Clostridium welchii* from a fatal case of gas gangrene was employed in this experiment. The technique of inoculation was the same in each case, one cubic centimetre of broth culture being injected into the macerated muscle of the right hind-quarter of the animal. In every case in which there was clinical evidence of the disease, *Clostridium welchii* was recovered in pure culture and identified by smears, cultures and rabbit inoculations. All dead animals were submitted to autopsy and photographed. In all the untreated animals not dying within the first thirty-six hours, the gangrenous process was much more extensive than in the treated animals. This was marked by extension of the gangrene into the deep muscles of the leg to the femur, while in the treated animals the disease in all cases extended no deeper than the superficial muscles. The mortality among the untreated animals was 86% and among those receiving therapy it was 25%. The amount of radiation given varied from 600 to 1,600 *r*, total dose; but the amount given is no criterion of the result obtained. Every treated animal was regarded as an individual case and treatment was given according to the severity of the disease and the general condition. It was found that recoveries were better and faster among the animals receiving an early initial treatment of 300 *r*, with a second treatment of at least 200 *r* within six hours. There was no absolute criterion for the therapy other than to treat early and adequately.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on October 19, 1944, at Saint Vincent's Hospital, Sydney. The meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital. Part of this report was published in the issue of March 10, 1945.

Progressive Muscular Atrophy.

DR. R. J. TAYLOR showed a girl, aged thirteen years, who eight months earlier had begun to notice that the third and fourth fingers of the right hand were assuming a position of flexion and she was unable to straighten them. One month later, weakness of the right shoulder with difficulty in abducting the arm was noticed, and there was wasting of the scapular region. The arm gradually became weaker and more wasted, until the condition on her admission to hospital was practically that of a flail arm. About two weeks before her admission to hospital on September 20, 1944, weakness of the left arm appeared, and she was soon unable to raise the arm above her head. There was no history of a similar complaint in other members of the family.

On examination of the right arm, considerable wasting was found in the deltoid, supraspinatus, infraspinatus and all the muscles of the arm, the forearm and the thenar and hypothenar eminences, as well as in the interossei. There was complete loss of motor power except for slight movement of the fingers. The limb was flaccid, all tendon reflexes were absent and sensation was unimpaired. Examination of the left arm disclosed slight wasting of the deltoid and spinati with considerable wasting of the thenar eminence and less wasting of the hypothenar eminence. There was generalized reduction in motor power throughout the arm. Tone was fairly normal, tendon reflexes were all present and sensation was unimpaired. On examination of the lower limbs, the only noteworthy feature was a decrease in power of the peroneal muscles and hamstrings of the left leg. Investigation of the cardio-vascular, respiratory and gastro-intestinal systems revealed no abnormality. The blood failed to react to the Wassermann test. X-ray examination revealed no evidence of cervical rib or other bony abnormality. Biopsy of muscle showed that there was no increase in connective tissue between the muscle fibres, which were mostly of small or normal size. Much loss of striation and some increase in sarcolemma nuclei had occurred. Also the sarcolemma substance had partly disappeared, so that there seemed to be broad transverse bands with pale areas between them. Dr. Taylor said that the interesting features of the case were the youth of the patient and the absence of fibrillary twitchings.

Syringomyelia.

Dr. Taylor then showed a male patient, aged thirty years, who when first examined on August 14, 1944, had complained only of difficulty in elevating the right arm. This condition had appeared about a week previously and had been of rather sudden onset. Until that time he had always enjoyed good health, and the only indication of any former trouble was the fact that the patient stated that he had "dragged" his left foot since his childhood and for about the last eight years had frequently burnt himself and tended to fumble things a little.

On examination, wasting of the deltoid, supraspinatus and infraspinatus on the right side was noticed. There was weakness of the muscles of the forearm, but no obvious wasting; the interossei were noticeably wasted. Dissociated anæsthesia (for pain and temperature) was present in both the upper limbs, and scars of old second-degree burns caused by leaning on steam pipes were present on both forearms. His hands had the strange, succulent, boneless feel said to be characteristic of syringomyelia. The knee and ankle jerks were exaggerated, and on both sides there was knee and ankle clonus and the plantar reflex was extensor in type. Dr. Taylor said that the interesting feature of the case was the improvement that had occurred as a result of vitamin B_1 and E therapy. At the time of the meeting there was, for the most part, only a blunting of perception to pain and temperature in the upper limbs. An area of anæsthesia was present over the left shoulder region, extending down to the level of the second rib anteriorly and to the top of the scapula posteriorly. In the legs, the findings were the same as before. The patient was able to carry out an almost complete range of movements with the affected arm, which was still wasted and weak; but he was very little hampered by the condition.

Polyposis of the Colon.

DR. I. D. MILLER first showed a pathological specimen, consisting of ascending, transverse and descending colon together with two inches of the terminal part of the ileum, to illustrate diffuse polyposis of the colon. The condition was familial, the patient's mother and brother having died of carcinoma of the colon at an early age. Dr. Miller said that the patient was aged thirty-four years, and had complained of the passage of blood and mucus *per rectum*. X-ray examination revealed the typical appearance, affecting the whole colon. A terminal ileostomy had been established, and the patient was being given the opportunity to determine whether this state was compatible with her normal existence. If she found that she could manage the ileostomy, the remainder of the colon was to be removed at a future date. The routine use of "Normocol" and attention to diet had resulted in the passage of about five formed stools in the twenty-four hours. Her present feeling was that the ileostomy was tolerable.

Arterio-Venous Aneurysm.

Dr. Miller then showed a female patient, aged thirty-six years, suffering from an arterio-venous aneurysm of the tibial vessels of her left leg. The patient had a history of varicose congestion of the left leg for the preceding nineteen years. During her first pregnancy eight years earlier, she suffered from ulceration of the left leg, which disappeared after childbirth, but returned with greater severity during a subsequent pregnancy three years later. After this, the ulcer healed and recurred every few months. In the last four years the patient had suffered from increasing pain over the upper aspect of the left tibia. The pain was worse after walking, and was intermittent and of aching or boring character. Pain was relieved by resting and keeping the leg raised. The leg, on examination, was found to be greater in all measurements than the other. There was an expansile swelling in the popliteal fossa, and the whole of the anterior tibial compartment had a strong expansile swelling and a thrill. The dilated peripheral veins pulsated with the arterial pulse; her general circulation showed the character of an aortic regurgitation.

Arteriography after the injection of "Perabrodil" into the femoral artery revealed a diffuse system of arterio-venous communication from the popliteal fossa down to the calf region. Considerable changes in the tibia, due to abnormal hyperæmia and vascular changes in the bone, was found. Operative interference was considered inadvisable unless there was some stronger symptomatic indication than existed at the time of the meeting.

Exophthalmic Ophthalmoplegia.

Dr. Miller finally showed two patients suffering from exophthalmic ophthalmoplegia. He said that most recorded cases of this condition were in some way related to thyreoid disturbance and frequently occurred after thyreoidectomy for Graves's disease. Neither of the patients shown was or had been clinically suffering from thyreotoxicosis, though there was some suggestion of the condition in the appearance of both of them. The most serious feature of the condition was its progressive and often acute course, threatening the vision of the eye. In the case of one of the two patients, inability to close the lids and considerable congestion of the orbital veins were present. An extensive transfrontal orbital decompression operation had been performed, with removal of the roof and lateral wall of the orbital cavity. Little recession of the eye had occurred, but the congestion had greatly subsided and the eye looked much better. Dr. Miller said that the essential pathological process was unknown. The orbital contents were always under great tension, and the muscles were much increased in bulk. As a rule there was small cell infiltration of the muscles; but this was not found in the present case. The ophthalmoplegias were due to mechanical factors within the orbital cavity.

Congenital Heart Disease.

DR. R. JEREMY and DR. R. L. SPEDDING showed four patients suffering from congenital heart disease.

The first patient was a woman, aged twenty-eight years, who had for years complained of dyspnœa on exertion. Her mother stated that she had been a delicate baby and had not been allowed to go to school. She had been cyanosed

to some degree at birth, and this condition had become more apparent since an attack of pneumonia at the age of six years. On examination, cyanosis was present with clubbing of the fingers. Clinical examination of the heart revealed slight enlargement to the left, but there were no cardiac murmurs. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure 85 on the right arm; the corresponding figures on the right leg were 140 and 100. Both femoral arteries were pulsating forcibly. A blood count showed that the erythrocytes numbered 5,700,000 per cubic millimetre, the hæmoglobin value being 125%. The blood failed to react to the Wassermann test. Radiological examination revealed the following facts: in the antero-posterior view the aortic knob was absent, the pulmonary arch was prominent and the left lower border contour suggested that it was formed by the right ventricle. Both pulmonary arteries and the intrapulmonary arteries were much enlarged and vigorously pulsating. In the right anterior oblique view, the left atrium did not appear to be enlarged; the broad, rounded top of the pulmonary artery was clearly seen; the aortic impression on the barium-filled œsophagus was small, while that of the pulmonary vessels was broad. Electrocardiographic examination revealed a pronounced right axis deviation. The patient was presumed to have a widely patent interatrial septal defect, probably associated with other congenital anomalies.

The second patient shown by Dr. Jeremy and Dr. Spedding was a girl, aged fifteen years, who complained of occasional tiredness, but who was otherwise quite vigorous and without symptoms. She was said to have had a "bad heart" when five years of age. Her general physical and mental state was excellent; the heart was not enlarged to clinical examination, but on auscultation a machinery murmur typical of patent *ductus arteriosus* was heard in the second left intercostal space. The systolic blood pressure was 100 millimetres of mercury and the diastolic 45 millimetres. Radiological examination revealed that the heart was of normal size, but there was some prominence of the pulmonary arch, which encroached on the aortic knob. The left atrium was not enlarged.

Dr. Jeremy and Dr. Spedding then showed a female patient, aged forty-three years, who was said to have suffered from rheumatic fever five years before, for which she was kept in bed for one week only. She now complained of dyspnœa on extreme exertion. Her general nutrition was good; no cyanosis or clubbing of the fingers was noted. There was some displacement of the apex beat to the left; a systolic murmur was present, maximal in the third and fourth left intercostal spaces, but also heard in the second left intercostal space; the pulmonary second sound was accentuated. The systolic blood pressure was 140 millimetres of mercury and the diastolic pressure 90. A blood count showed that the erythrocytes numbered 4,410,000 per cubic millimetre and the hæmoglobin value was 85%. The blood failed to react to the Wassermann test. A radiological examination was carried out. In the antero-posterior view moderate general enlargement of the heart was revealed; there was considerable enlargement of the pulmonary arc, the pulmonary arteries and the intrapulmonary vessels. The aortic knob was visible. Fluoroscopic examination revealed that the hilar vessels and the intrapulmonary vessels pulsated vigorously; the left atrium was not enlarged. An electrocardiographic examination revealed right axis deviation with slurring and notching of the *QRS* complexes. It was presumed that the patient had Eisenmenger's complex, with patent interventricular septum, dextroposition of the aortic orifice overriding the septal defect and right ventricular hypertrophy.

Dr. Jeremy and Dr. Spedding next showed a female patient, aged thirty-six years, who was said to have had a heart murmur at the age of five years, and at sixteen years of age to have had rheumatic fever. She had been breathless on exertion for years, and also complained of giddiness on walking. The heart did not appear to be enlarged. There was a loud murmur occupying the whole of the systole; it was maximal over the fourth left intercostal space, was also heard up to the second left intercostal space and was fairly loud at the cardiac apex and fainter toward the axilla. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure 90. A radiological examination was made. In the antero-posterior view the aortic knob was seen to be small, the pulmonary artery was slightly prominent and the heart was not generally enlarged. In the right anterior oblique view, the pulmonary conus appeared to be enlarged, but the left atrium was normal. Electrocardiographic examination showed no axis deviation. It was presumed that the patient had a patent interventricular septum, Roger's disease. The question of concomitant acquired rheumatic valvular disease arose, but was considered to be answered in the negative by the absence of left atrial enlargement.

Myotonia Atrophica.

Dr. Jeremy and Dr. Spedding finally showed a male patient, aged thirty-nine years, complaining of weakness of the forearms and hands of five years' duration and of the legs of ten years' duration. An unmarried brother had been similarly affected from the age of thirty years; he was fairly bald and had recently died from a ruptured appendix. A step-sister developed cataract at the age of forty years. The patient had two children, and had been proud of his strength until his late twenties; he was a good athlete in his youth. He has become moderately bald in the past ten years. His sexual power had been diminishing in the past two years; he was able to manage coitus only after sleep. In reply to a leading question, he stated that about two years earlier he had begun to find it difficult to reopen his hands after a handshake, and that he thought that his muscles had twitched occasionally in the past few years.

Examination revealed the patient to be a medium-sized man of about his stated years, with a somewhat expressionless face and speaking with a slightly nasal intonation. Wasting of the sterno-mastoids and neck muscles, the muscles of both forearms and arms, the dorsiflexors of both feet and the left posterior calf muscles, and a slight wasting of the vasti of both thighs was present. There was weakness of the muscles of the back, and there appeared to be slight weakness of the facial muscles. No sensory changes could be detected. The knee jerks were difficult to elicit. The left ankle jerk was absent; the right ankle jerk was occasionally elicited. In the upper limbs, the right triceps jerk was weak, but present, and the others were absent. The abdominal reflexes were brisk and the plantar reflexes were flexor in type. The intrinsic muscles of the hands and feet were intact. Early cataract was present in both eyes. After handshaking, the thumb did not relax as quickly as the other fingers. This was the only sign of myotonia. The blood failed to react to the Wassermann test. In the differential diagnosis, peroneal muscular atrophy was considered; but it was thought that the diagnosis of *myotonia atrophica* was made fairly certain by (i) wasting of the sterno-mastoids and neck muscles, (ii) absence of involvement of the intrinsic muscles of the hands and feet, (iii) weakness of the back muscles, (iv) the family history, (v) the baldness, (vi) the presence of early cataract, (vii) the suspicion of myotonia in the right thumb, and (viii) the absence of sensory loss.

(To be continued.)

NOTICE.

THE General Secretary of the Federal Council of the British Medical Association in Australia has announced that the following medical practitioners have been released from full-time duty with His Majesty's Forces and have resumed or will resume civil practice as from the dates mentioned:

Dr. A. J. Aspinall, 135, Macquarie Street, Sydney. (April, 1945.)

Dr. S. G. Bradfield, 400, Chapel Road, Bankstown. (February, 1945.)

Dr. Charles F. Marks, 109, Wickham Terrace, Brisbane. April 1, 1945.)

Public Health.

A SCHOOL OF NUTRITION AT CANBERRA.

As announced recently by the Minister for Health, Senator the Honourable J. M. Fraser, the Commonwealth Government has decided to establish a School of Nutrition at the Institute of Anatomy, Canberra.

Lectures for the 1945 course will commence on April 3. Because of limitations of space and teaching staff the class will be restricted to twelve persons.

The purpose of the school is to train teachers at schools of domestic economics, technical schools and universities in nutritional science, and to provide training for persons who could undertake nutrition work in the various fields of public health.

Persons eligible for enrolment will include: (*a*) medical graduates, (*b*) university graduates in science who have

completed a course in biochemistry, (c) hospital dietitians, (d) persons having qualifications considered to be the equivalent of any of the above.

The course of instruction will occupy about nine months and will be in two parts. Part I will include instruction in: the principles of nutrition; nutrition in relation to public health; agriculture in relation to nutrition; food and dietetics; the applied nutrition of infants, children and other specialized groups in the community; as well as such related subjects as applied psychology, production and marketing of food, elementary statistics. The students will be required to conduct animal experiments to study the effects of vitamin deficiencies. Part I will occupy about six months.

In Part II the students will be required to conduct field studies and surveys to familiarize themselves with conditions existing in various parts of Australia.

The Government has decided to make available six scholarships for persons eligible to undertake the course of instruction. The scholarships are valued at £150, and, in addition, a living allowance of 30s. per week will be paid during the course.

It is emphasized that the course of instruction is open to persons with the necessary qualifications other than those awarded scholarships. The transport expenses and fares of all students whilst taking part in the field studies and surveys will be paid. Full particulars of the course may be obtained from the Director, Institute of Anatomy, Canberra.

Medical Practice.

PRESCRIPTIONS CONTAINING DANGEROUS DRUGS: AN AMENDING REGULATION IN NEW SOUTH WALES.

THE following letter has been received from the Chief Secretary's Department, New South Wales.

Dear Sir,

I am enclosing for your information a copy of a notification published in the *Government Gazette* on the 9th February, 1945, amending Regulation 19 (3) (*b*) under the *Police Offences Amendment (Drugs) Act*. The Regulation as it now stands is quoted hereunder, the amendment being underlined:

"19. (3) The following conditions shall be observed by persons dispensing any such prescription for or supplying a drug upon any such prescription:

. . . . . .

(*b*) The person who dispenses a prescription which does not clearly indicate the maximum number of times such prescription is to be dispensed or which has reached the last occasion upon which it can be legally dispensed according to the maximum indicated thereon shall write, stamp, or mark in legible letters across such prescription the word 'cancelled', shall retain such 'cancelled' prescription and shall preserve the same on a file for two years."

The amendment makes it obligatory upon a dispensing chemist to retain on a file for two years any prescriptions containing dangerous drugs. As the law stood before, although many chemists did retain such prescriptions, the prescriptions could not be lawfully retained if their return were demanded by the persons on whose behalf they were dispensed.

Yours faithfully,

S. L. ANDERSON,
Under Secretary.

Chief Secretary's Department,
Sydney,
February 27, 1945.

Correspondence.

MEDICAL EDUCATION IN INDIA.

SIR: Plans have recently been completed to strengthen and hasten the progress of medical education in India by adding to its medical schools a first-grade Christian medical college at Vellore, Madras Presidency, India. Attached to the college is a hospital and nursing training school.

Twenty-eight missionary societies in Britain and America and the European continent have united in this enterprise. Large plans for buildings and staff are being carried into effect. A staff of a dozen British and American teachers with their Indian colleagues is already at work. Australia is represented by Edward Gault, M.D., M.S. (Melbourne), F.R.A.C.S., and Mrs. Gault (a medical graduate of Sydney University).

A meeting of the Melbourne "Friends of Vellore" is to be held on Friday, March 23, at 8 p.m., in the Reception Room (second floor), Assembly Hall, Melbourne. Miss E. Rivett, M.A., Principal of the Women's Christian College, Madras, will speak on the subject: "Vellore Medical College." Medical men and women are cordially invited.

Yours, etc.,

C. I. MCLAREN.

4, Barry Street,
Kew, Victoria,
February 20, 1945.

WHITE RACE IN THE TROPICS.

SIR: The editorial of January 27, 1945, is not altogether fair in dismissing the amount of attention given to this problem in Australia as negligible, as a good deal of work has been and is being done on the forces. The results appear largely as official documents circulated amongst those most concerned. Nobody has had time to compile a general account of this work; in fact, at this stage of the investigation caution would have to be exercised in any such attempt. Nevertheless, more could be done if the means were available.

We are, of course, handicapped in Australia by lack of equipment and lack of manpower. We have, as a nation, never encouraged medical research on a broad front, and there is still too much rejoicing over the diversion of promising youths from the adventure of scientific inquiry to the solid security of medical practice. The general lack of scientific manpower is, therefore, the fruit of our past behaviour. How long we shall continue to gather this fruit I do not know. The special lack in the field of tropical physiology is aggravated by the comparative newness of the subject. Australia's role in its development has not passed unnoticed, so that some recruits may be attracted to it.

I would utter a strong caution against books written by pundits resident in temperate climates. Visits to the tropics and experiments conducted on unacclimatized personnel give a warped view of the actual possibilities, while an appeal to history can yield no more than a condemnation of our past casual approach to an important and difficult problem. Already our tropical operations have shown that opinions based mainly on these approaches must be treated with a great deal of reserve.

Yours, etc.,

DOUGLAS H. K. LEE,
Professor of Physiology.

University of Queensland,
February 21, 1945.

PHARMACEUTICAL BENEFITS ACT, 1944.

SIR: We quote the masterly conclusion of newsletter 8 of the British Medical Association (Victorian Branch) in reference to the *Pharmaceutical Benefits Act*:

> At the moment there is a lull in the Government's attack on the standard of medical practice in Australia as it seems to have diverted its attention to bigger game—the Banks and the Airways—but that lull is only temporary and members need have no illusions regarding the voracity of the Socialistic tiger.

We are in complete agreement with the objections of the Federal Council to the *Pharmaceutical Benefits Act*, 1944, and feel that the motives which prompted its reasoned resolutions were inspired by a desire to protect the patient and that latitude in individual prescribing which is necessary in the patient's interest. Whatever our political and sectarian beliefs may be, we cannot see any justification for the inclusion of a grim warning against the "voracity of the socialist tiger". These sentiments introduce an issue which obscures and misrepresents the basis of the medical profession's objections to an unjust and dangerous act and openly invite accusations of "protected interests", "capitalistic lion" and "trade unionism", which are the substance of most attacks on the British Medical Association. Why, oh why, are these worthless political red-herrings thrown

across the path of a grave subject on which there has been published mature and impartial judgement?

After a prolonged period of service, sheltered from the facts of life, we are supposedly ignorant of the disturbing medico-political undercurrent which threatens the established order of medical practice. We suspect that the end of our string leads to the same central tangle as that of civilian practitioners, but we must be silent about it. Probably because of this ignorance, we cannot, for the life of us, see the relationship of a socialistic tiger and the proposed pharmaceutical act; dispassionate and disinterested resolutions have been issued by the Federal Council, yet this dangerous irrelevant claim is hurled at those people who are prepared to base any conclusions on an ill-considered statement. They are entitled to under the circumstances.

We are prepared to believe that many medical men (and women) are disinterested in the practice of their profession and that the ideals they glimpse in the Hippocratic oath are remembered as something more than a dreary incantation that is mumbled toward the end of a medical course. In any case, a detached scientific evaluation should not be cheapened by inconsequential political catch-phrases.

Yours, etc.,

H. M. FISHER,
Colonel, Australian Army Medical Corps.
GEORGE READ,
Major, Australian Army Medical Corps.
THOMAS WALPOLE,
Captain, Australian Army Medical Corps.

Headquarters,
Sixth Australian Division,
February 20, 1945.

SIR: Dr. Lawes has concluded that the *Pharmaceutical Benefits Act* will confer real benefits on the community. Of course it will, but the benefits will be financial ones only. These financial benefits will be appreciated by the poor who receive domiciliary treatment. The bulk of the Australian people today is in well paid employment, and can well afford to pay for most medicines. There can be no claim, therefore, that the financial benefits conferred by this Act are in urgent demand. In fact, there has been no demand for them at all, and most Australians never heard of "pharmaceutical benefits" until the Bill was in preparation.

The Government has introduced the measure because of a political belief that medicine should be free. Dr. Lawes has displayed such facility in explaining the Government's motive, and such confidence in predicting the future governmental programme, that one may be pardoned for suspecting that he, also, is interested in the scheme on political, rather than humanitarian, grounds. As a matter of fact, humanitarianism does not enter into the dispute. Any argument to the contrary is sheer sophistry. Should any person be inconvenienced because of our refusal to cooperate with the Government, the fault will be with the Government. The Government has the power and the money to pay for all prescriptions, but it refuses to do so. We have asked them to pay for anything we may find it necessary to prescribe. The public therefore cannot accuse us of not considering its interests.

It is strange to find that some of our members still ask why we will not cooperate in what should be described as the Government Partial Pharmaceutical Benefits Scheme. They ask further why, if we insist on a complete scheme, we will not cooperate in a partial scheme, on the principle that half a loaf is better than no bread. The reason is an important one. To cooperate in a partial scheme would involve the sacrifice of our freedom in prescribing. The partial scheme must of necessity mean that pressure will be exercised upon us, by our patients and the Government alike, to confine our prescribing to the formulary. The principle is involved, no matter how wide the formulary may be.

The Government knows what it is doing. This is the first shot in the battle to socialize medicine. The Government is cleverly manœuvring for position. If it can manœuvre us into the position of abandoning, on specious pretexts, any portion of our freedom, it will be well on the way to victory.

I appeal to our members to remain loyal to their Council in this matter. The Council has a difficult and responsible task to perform—that of protecting the interests of a freedom-loving profession against attempts to socialize it. It is easy enough to be loyal to our Association in fair weather. True loyalty is that which is displayed in times of stress. Of one thing I am certain—if the whole profession will remain loyal in responsing to the Federal Council's plea for non-cooperation, the Government will be compelled to admit the principle of freedom in prescribing, and will be slow to attack our freedom in any other direction. The result will be a real benefit to the public.

Yours, etc.,

A. J. COLLINS.

185, Macquarie Street,
Sydney,
March 5, 1945.

SIR: Recent letters published in the journal, critical of the policy of the British Medical Association in its relations with the Government, do not, I feel sure, represent the views of the great majority of the profession. At a time like this, when loyal support of our selected leaders and delegates is essential if we are to survive as an ethical profession, it would be the height of folly to allow the noisy minority to think the great body of opinion is behind it. After long negotiations between our councils and the bureaucratic and political machines, a climax approaches now with the date of the "Free Medicine" Bill announced: the implementation of which is, I feel sure, the thin edge of the wedge to divide and separate us when all the other national insurance ideas are due to be tried. There has been plenty of time for us to express our views and for all the pet criticisms to be trotted out, and there have been plenty of opportunities too—conventions (at which the services were represented) and Branch meetings have been held and the pages of this journal have been open to all of us—to express our relevant or irrelevant opinions. At this late stage, with the fight due to commence in about three months' time, it is too late to allow of any dissension at all appearing in our ranks. We are really only concerned with the main issue, whether the bureaucrat is to control the profession in Australia. All these idealistic and "sob stuff" anxieties and worries about how the patient will fair without his bottle of free medicine are really quite beside the main point which interests us all. The patient will get his treatment, never fear, and doesn't appear to be worrying very much himself. We will treat him and give him his prescription; but if then, for some political or bureaucratic reason, he cannot have it dispensed, the onus appears to me to be on the Government; we will tell him what to do and if they won't let him do it, that is no fault of the doctors. Anyhow, he manages quite well now without the pharmaceutical bill and without the redoubtable formulary. All these letters, going over the same arguments again and again, in spite of any answers and explanations given, can do nothing now to help; they will be fastened on by Government spokesmen to point out dissension in our ranks and to weaken the Federal Council's position, and will be used to help whispering campaigns and rumour-carried propaganda to create suspicion and distrust amongst us.

I don't think anybody has any real doubts about the merits of the Federal Council's attitude to the pharmaceutical bill and to the national insurance problem in general, but I do think there is considerable uneasiness about our loyalty to each other; there is a very real fear that the other fellow will start using the formulary and that the man who sticks loyally by the Association will be left out in the cold. There can be no doubt of the result if we remain united; we all know that. The time has come, sir, to ask for a pledge of support from each member. Let the Federal and Branch Councils take an uncompromising stand and demand one immediately and then we will all know where we stand when the "heat comes on". Wordy arguments and criticisms are quite out of place; we are up against it and we can only win if we pledge ourselves to unity and unswerving loyalty.

Yours, etc.,

CAWLEY MADDEN.

"The Oaks",
517, Pacific Highway,
Killara, New South Wales.
March 6, 1945.

HOUSEWIVES' DERMATITIS.

SIR: In the issue of the journal, February 17, 1945, your leader, "Housewives' Dermatitis", opens up a large field for endeavour.

The wife's calling is an occupation which is not given its proper recognition. What is the profession doing to help the housewife? Just nil.

If, as your article suggests, the only way of attacking housewives' dermatitis is to badger an already harassed Government to grant priorities for rubber gloves, I think you had best give up the ghost before you start.

One reads in the journal about preventive medicine; but it appears that prevention does not apply where large interests are concerned, for I think most practitioners will agree that these cases of dermatitis were not nearly so prevalent before the use of the much advertised soap powders and other such easy aids to housekeeping. Prohibit the manufacture and sale of these products and see what happens. If you do there will be no need to "Rubb'er for Victory".

Yours, etc.,

J. BRUCE GORDON.

Rockhampton,
Queensland,
February 22, 1945.

Naval, Military and Air Force.

APPOINTMENT.

THE undermentioned appointment has been promulgated in the *Commonwealth Gazette*, Number 43, of March 1, 1945.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Extension of Appointment.—The appointment of Surgeon Captain William James Carr, C.B.E., is extended for a period of one year from 30th January, 1945, under the provisions of the National Security (Naval Forces) Regulations.

CASUALTIES.

WE regret to anounce the death of Major-General Rupert Major Downes, which occurred on March 5, 1945, near Cairns, Queensland.

We regret to announce the death of Colonel Robert Heathcote Russell, A.A.M.C., which occurred on March 5, 1945, near Cairns, Queensland.

Nominations and Elections.

THE undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Bernard, Charles ffranks, M.B., B.S., 1929 (Univ. Sydney), 73, Wyong Road, Cremorne.

Cunynghame, Donald Dryborough, M.B., B.S., 1942 (Univ. Sydney), Flight-Lieutenant D. D. Cunynghame, 29, Harrow Road, Auburn.

Gibson, Richard Maxwell, M.B., B.S., 1944 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Gollan, Keith Ransome, M.B., B.S., 1944 (Univ. Sydney), Keerrong, Pennant Hills Road, Parramatta.

Milson, Anthony Howard, M.B., B.S., 1944 (Univ. Sydney), 15, Walloroy Road, Double Bay.

Peate, Desmond Lees, M.B., B.S., 1939 (Univ. Sydney), 53A, High Street, Waratah.

Pennington, Victor Warren, M.B., B.S., 1941 (Univ. Sydney), 266384, Flight-Lieutenant V. W. Pennington, 52, Knox Street, Randwick.

Pendergast, James Robert, M.B., B.S., 1944 (Univ. Sydney), St. Vincent's Hospital, Darlinghurst

Quill, Jack Sidney, M.B., B.S., 1944 (Univ. Sydney), 61, Railway Street, Carlton.

Books Received.

"Hypertension: A Manual for Patients with High Blood Pressure", by Irvine H. Page, A.B., M.D.; Fourth Printing; 1944. Springfield: Charles C. Thomas. 7¼" × 5", pp. 92, with seven illustrations. Price: $1.50, post paid.

"Bibliography of Industrial Hygiene", Volume XIV; 1940. Geneva: International Labour Office. 9¼" × 6¼", pp. 168. Price: 6s.; $1.50.

"Recent Advances in Endocrinology", by A. T. Cameron, M.A., D.Sc. (Edinburgh), F.R.I.C., F.R.C.S.; Fifth Edition; 1945. London: J. and A. Churchill Limited. 8" × 5", pp. 422, with 90 illustrations. Price: 18s.

"Statistical Methods for Research Workers", by R. A. Fisher, Sc.D., F.R.S., D.Sc. (Ames, Harvard), L.L.D. (Calcutta); Ninth Edition; 1944. London: Oliver and Boyd Limited. 8" × 5", pp. 363, with illustrations. Price: 16s. net.

"Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases", by Richard P. Strong, M.D., Sc.D., D.S.M., C.B.; Seventh Edition, Volume II; 1944. Philadelphia: The Blakiston Company. 9" × 6", pp. 922, with many illustrations. Price: $21.00 per set.

"Arterial Injuries: Early Diagnosis and Treatment", by the Vascular Injuries Subcommittee of the Medical Research Council War Wounds Committee; 1944. London: His Majesty's Stationery Office. 10" × 6", pp. 24, with 7 illustrations. Price: 4d. net.

Diary for the Month.

MAR. 19.—Victorian Branch, B.M.A.: Hospital Subcommittee.
MAR. 19.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
MAR. 20.—Victorian Branch, B.M.A.: Organization Subcommittee.
MAR. 20.—New South Wales Branch, B.M.A.: Council Quarterly Meeting.
MAR. 21.—Western Australian Branch, B.M.A.: General Meeting.
MAR. 22.—New South Wales Branch, B.M.A.: Annual Meeting.
MAR. 23.—Queensland Branch, B.M.A.: Council Meeting.
MAR. 27.—New South Wales Branch, B.M.A.: Council Meeting.
MAR. 28.—Victorian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All Public Health Department appointments.

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